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Lung Abscess Secondary to Aseptic Pulmonary Infarction[1]

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ELEVEN INSTANCES of lung abscess secondary to aseptic hemorrhagic pulmonary infarction were encountered in a recent study at Cleveland City Hospital (6). This complication especially interested us because in certain cases the symptoms and signs of lung abscess so dominated the clinical picture that the underlying infarct had been unsuspected, to be disclosed only at autopsy.

The literature contains numerous articles on the subject of pulmonary infarcts, but only an occasional reference to possible occurrence of a secondary abscess in an infarct. It is well known that aspiration of infected material may cause a lung abscess; also, that septic emboli are almost certain to be followed by abscess formation. It appears, however, that aseptic pulmonary infarction as a cause of lung abscess is not generally appreciated. Indeed, Castleman (1) has said that superimposed infection of a pulmonary infarct is a rare coincidence.

In discussing the pathogenesis of lung abscess, Lilienthal (7) pointed out that an infarct may be infected by the embolus itself or secondarily contaminated from the bronchial tree, so that an abscess is produced.

Van Allen and his associates (12), working with dogs, were able to produce only an occasional lung abscess either by means of sterile emboli (bird shot) or by intrabronchial insufflation of infected material. When they combined both methods in the same animal, however, they produced abscesses with much greater frequency. They concluded that a certain percentage of all abscesses are produced in this manner, *i.e.*, bronchogenic infection of an aseptic infarct.

Cutler and Gross (2) pointed out that an infarct is an excellent site for the formation of an abscess, and that this is quite likely to occur if pathogenic organisms are present in the bronchial tree.

Steinberg, Clark and de la Chapelle (10) reported four autopsied cases of empyema following necrosis of bland infarcts in patients with cardiac disease. Hollmann (4) described the case of an elderly woman with a large abscess in the left upper lobe, which proved at autopsy to be in the center of a large infarct. Marks (9) recorded two examples of pneumothorax following pulmonary infarction.

Touroff (11) reported a single case of "infrapulmonary" empyema due to necrosis of an infarct. The empyema was successfully treated by rib resection and drainage.

Kirklin and Faust (5) in 1930 observed that secondary abscesses may occur and obscure the clinical and roentgenologic picture. Gsell (3) also mentioned the possibility of secondary infection of a bland

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infarct with abscess formation or gangrene, and reported one case.

CLINICAL OBSERVATIONS

Some or all of the usual signs and symptoms of pulmonary infarction were present in every case in which a lung abscess eventually developed. These included hemoptysis, chest pain, dyspnea, pleural friction rub, and signs of consolidation.

The distinguishing clinical feature in these cases with abscess formation was the occurrence of a foul, purulent sputum some days or weeks after the onset of the infarct. It was usually accompanied by a secondary rise in temperature and an elevation of the leukocyte count. In patients with heart disease, an increase in the severity of the cardiac failure followed.

The clinical picture was very similar to that described by Lord (8), who stated that "abscess formation or gangrene may develop at the site of an infarct. In the presence of such pulmonary complications, the sputum changes in character and, in addition to blood from the infarct, contains pus, which may be foul, and elastic tissue. Empyema or pneumothorax may complicate the destructive pulmonary changes."

ROENTGENOLOGIC CONSIDERATIONS

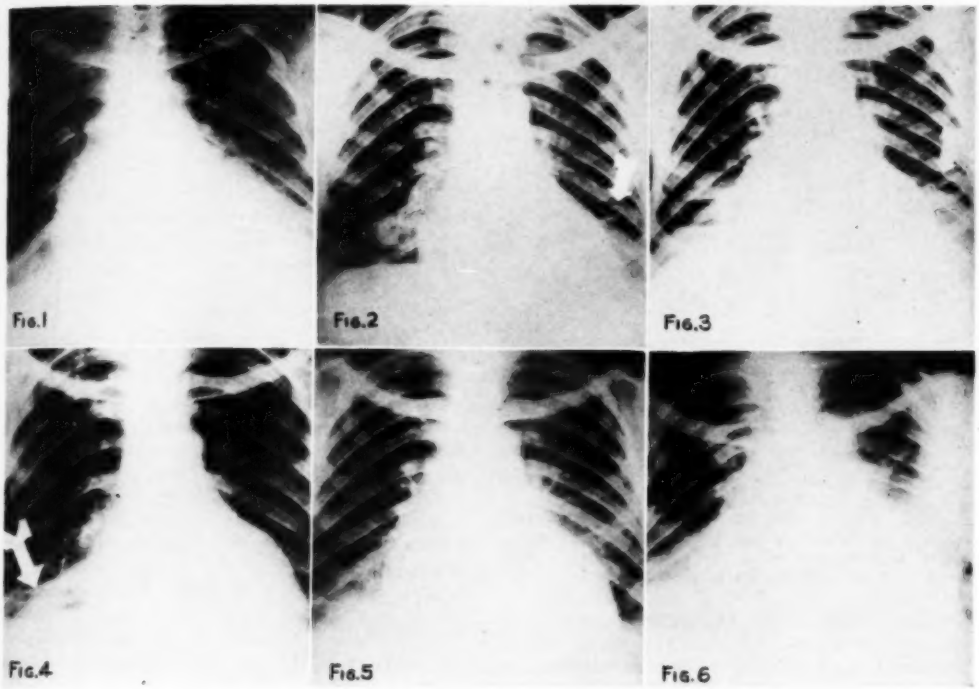
The observations of previous authors as to the appearance of the infarct shadow have been confirmed. Roentgenologically the infarcts varied widely in appearance, depending on size, position, age, and presence of secondary infection, pleural effusion, or passive hyperemia. This is demonstrated in Figures 1–18. The typical triangular appearance of the infarct seen on the postmortem table was not demonstrated on the roentgenogram unless the central ray happened to pass through the infarct at right angles to its long axis. (If oblique and lateral views are made, this triangular shape will be seen with greater frequency.) The infarct shadow was usually in the lower portion of the lung field and in its early stages was often sharply demarcated except at the medial border. (An infarct is always adjacent to a pleural surface, either peripheral or interlobar.) In some instances the infarct shadow became fuzzy due to secondary bronchopneumonia; in others the infarct was obscured, or even hidden, by a pleural effusion. In all of the cases here reported it became the site of an abscess.

If the patient was first seen after an abscess had formed, with or without a pulmono-pleural fistula, the appearance of the secondary infection completely masked the underlying infarct. In such cases the clinical history was of great help in arriving at the correct diagnosis. (It is therefore important to consider the possibility of an infarct as the underlying cause in all cases of lung abscess, especially if cardiac failure is present.) When the patient was seen early in the course of his disease and was followed by serial roentgenograms, the diagnosis of lung abscess secondary to an infarct was relatively easy.

CASE REPORTS

A total of 344 instances of aseptic hemorrhagic pulmonary infarction were seen at autopsy during a ten-year period (1930–1939) at Cleveland City Hospital (6). In 174 of these cases the infarct was a significant cause of death. Eleven of the 17 cases which form the basis of this report were drawn from the latter group. The other 6 cases have since been studied on the wards and the correct diagnosis made ante mortem. Four of the 6 patients died in the hospital, and all came to autopsy. Two patients survived the acute illness but died several months later. In one of the latter, who had had surgical drainage of an empyema, autopsy was done. Thus 16 of the 17 cases were proved by postmortem examination.

In selecting our cases we have not considered simple necrosis in the center of an infarct as an abscess. The diagnosis of an abscess was made only when a cavity was present in the lung parenchyma. It must be borne in mind that all cases of blood stream infection have been excluded from this study, so that all infarcts which oc-



Figs. 1–6. Case 1: With typical signs and symptoms of pulmonary infarction; abscess formation demonstrable roentgenographically.

Fig. 1. Fifteenth hospital day, patient recumbent. The cardiac shadow is very large, obscuring the lower part of the left lung. Because of this, the clinically diagnosed infarct cannot be seen. Some passive hyperemia is present.

Fig. 2. Forty-second hospital day. The cardiac shadow is now much smaller. In the lower third of the left lung is a cavity showing a fluid level (arrow). In the lower third of the right lung field is a rounded shadow of increased density. A small pleural effusion is present in both costophrenic sinuses. By this time the sputum had risen to a volume of 500 c.c. daily, and was distinctly foul.

Fig. 3. Fifty-third hospital day. The abscess cavity on the left is somewhat smaller (arrow). There is now a well defined cavity at the right base, with infiltration around it. The sputum volume had decreased slightly by this time.

Fig. 4. Eighty-first hospital day. The abscess cavity at the right base is now smaller (arrow). The sputum volume was now much less.

Fig. 5. The 153rd hospital day. Both abscess cavities are closed. There remains some pleural thickening on both sides in these areas. At this time, except for a very mild cardiac failure, the patient was well. The foul sputum was no longer present, and the abscesses were considered healed.

Fig. 6. The 388th hospital day, patient recumbent. Anteroposterior view of the chest, showing the middle third of the left lung to be the seat of a homogeneous infiltration. This coincided with an area of consolidation found clinically and represented another infarct. The patient died eleven days later.

curred can be presumed to have been aseptic at the time of onset.

Pulmono-pleural fistula with empyema occurred 7 times in this group of 17 patients. In only 3 of the 17 cases was the infarct (and abscess) in an upper lobe.

The following 4 cases are representative of the group. A fifth case was described previously (6).

CASE 1: M. C., a 36-year-old female, known to have hypertension and coronary artery disease, was admitted to the Medical Service on May 3, 1939, in moderately severe cardiac failure, which responded to digitalis and mercurial diuretics. On the thirteenth hospital day the patient had a small hemoptysis, the temperature rose to 39° C., and she complained of pain in the left side of the chest. (See Figure 1, taken on the fifteenth hospital day.) On the nineteenth hospital day she experienced pain in the right side of the chest, and a friction rub was audible at the right base.

The cardiac failure persisted and there was little change in her now febrile course until the thirty-fifth hospital day, when the sputum, which had been

Fig. 7. Case 1: Section through the fixed left lung showing an infarct in the lower lobe, containing a cavity measuring 4 × 2 × 1 cm. (arrow). There was no communication with the pleural space

purulent, became foul. At this time signs of consolidation were present at both lung bases, and the previously small sputum volume increased to as much as 500 c.c. daily. (See Figure 2, taken on the forty-second hospital day, which demonstrates an abscess in the left lung.)

The large volume of foul sputum gradually decreased over a period of several weeks, but roentgenograms (Figs. 3, 4, and 5) revealed the development of an abscess in the right lung, followed by closure of both abscesses. By the 150th hospital day the patient was afebrile, and had almost no sputum, but a slight degree of cardiac failure persisted.

On the 262nd hospital day another hemoptysis occurred, accompanied by pain and signs of consolidation in the left side of the chest. From this time on the patient's condition became progressively worse, and her cardiac failure more severe. Several blood cultures showed no growth. On the 388th hospital day another roentgenogram (Fig. 6) revealed consolidation in the middle third of the left lung. Death occurred on the 399th hospital day, in severe cardiac failure. The significant autopsy findings were arteriolar nephrosclerosis, a 550-gram heart, containing thrombi in the right atrium, and several old and recent infarcts in both lungs. One of these, in the left lower lobe, contained an irregular cavity measuring 4 × 2 × 1 cm. (Fig. 7). Other infarcts showed fibrosis.

Comment: This patient had the typical signs and symptoms of repeated pulmonary infarction. Abscess formation was indicated by the appearance of foul sputum and by the roentgenographic findings. Although these abscesses healed, further infarction and abscess formation occurred, resulting in accentuation of the cardiac failure and death.

CASE 2: T. J., a 41-year-old colored laborer, was admitted to the Medical Service on May 1, 1939, with symptoms of myocardial insufficiency of five weeks' duration. He also complained of a pleuritic type of pain in the left side of the chest, and of a cough, productive of a thick, yellow sputum occasionally streaked with blood.

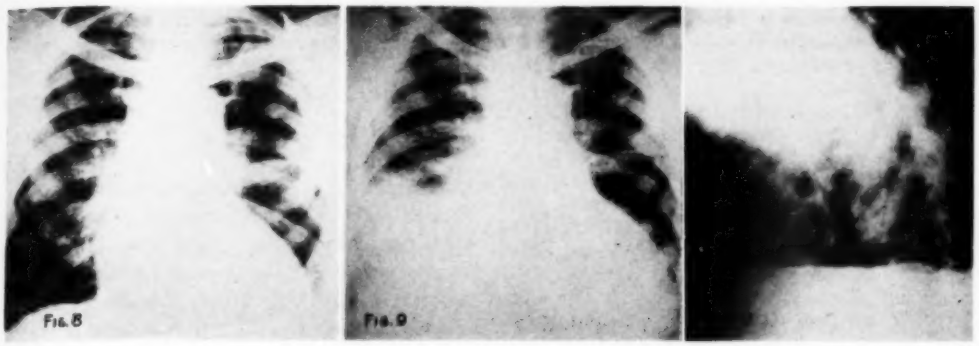
Physical examination revealed a large heart, with a to-and-fro murmur over the aortic area, and a moderate degree of cardiac failure. The blood pressure was 170/110 and the cardiac rhythm was regular. The leukocyte count was 6,000. The blood Kline and Wassermann reactions were 4+. Figure 8 is the admission roentgenogram.

The congestive heart failure responded fairly well to digitalis and mercurial diuretics until the sixteenth hospital day. At that time the patient complained of a pain in the right side of the chest and expectorated a small amount of blood. The temperature rose to 38.5° C. and the leukocyte count to 19,300. Later that day a pleural friction rub was heard over the right side of the chest and a thrombosed antecubital vein was noted. Figure 9 shows the infarct in the lower half of the right lung.

Four days later, on the twentieth hospital day, signs of fluid in the right pleural space were present. On the twenty-fourth hospital day the patient raised a large amount of foul, purulent sputum. The temperature now rose to 39° C. daily. Three blood cultures showed no growth. On the twenty-eighth hospital day a lateral roentgenogram of the chest (Fig. 10) revealed a fluid level in the pleural space. The patient died the same day.

At autopsy the cause of the cardiac enlargement was considered to be arteriolar nephrosclerosis. Syphilitic aortitis was present. Pulmonary infarcts were present in both lower and the right middle lobes. One of these, in the right lower lobe, contained an abscess measuring 6 × 3.5 × 3 cm. Through a pulmono-pleural fistula, this abscess communicated with a pyopneumothorax pocket containing 1,600 c.c. of a thick, greenish-yellow, foul pus.

Comment: This is a typical example of a bland infarct followed by secondary abscess formation, pulmono-pleural fistula, and pyopneumothorax. The clinical course was that of overwhelming infection. Although the fluid in the pleural space prevented visualization of the abscess, its presence was correctly diagnosed by the clinical findings.



Figs. 8–10. Case 2: Typical example of bland infarct followed by secondary abscess formation, pulmono-pleural fistula, and pyopneumothorax.

Fig. 8. First hospital day. There are streaked shadows of increased density near the left hilus which probably represent a healing infarct. Some passive hyperemia is present The appearance of the cardiac shadow (large left ventricle) is consistent with the clinical diagnosis of hypertensive heart disease. Note that the right lung is clear.

Fig. 9. Seventeenth hospital day. In the lower third of the right lung there is now a confluent mottling with slight streaking at the upper border. This represents a large infarct. There is no change in the appearance of the left lung.

Fig. 10. Twenty-eighth hospital day. Right lateral view of the chest, showing a fluid level in the right pleural space. A postero-anterior view, not shown, revealed an almost complete collapse of the right lung, with pyopneumothorax. At autopsy the same day, 1,600 c.c. of pus were found in the pleural space.

Fig. 11–13. Case 3, in which diagnosis was established by classical clinical signs and the roentgen appearance.

Fig. 11. First hospital day. In the lateral portion of the right mid-lung is an ovoid, sharply demarcated shadow of increased density, representing an infarct. The cardiac shadow is enlarged. There is a small pleural effusion at each base.

Fig. 12. Second hospital day, first oblique position. In this view the infarct is seen to be definitely triangular in shape and to lie in the right upper lobe, just above the interlobar septum. This triangular appearance is seen in only one projection in any infarct. Unless roentgenograms are made in more than one position, the diagnosis may be missed.

Fig. 13. Twentieth hospital day. A pneumothorax is seen on the left (following thoracentesis). There are definite areas of diminished density in the infarct in the right upper lobe (arrow), representing abscess formation. It was not until several days later that the sputum became foul and increased in volume.

CASE 3: W. H., a 51-year-old white male, was admitted to the Medical Service on June 4, 1940. His history revealed evidence of slight cardiac failure for about one year, during which time he had had several small hemoptyses and some substernal oppression. On admission he had a cough, productive of about 100 c.c. of rusty purulent sputum daily. He was in moderately severe cardiac failure, with signs of consolidation and fluid at both bases. The heart was enlarged to the left; a gallop rhythm and pleuropericardial friction rub were present. The blood pressure was 130/90. The cardiac failure was due to coronary sclerosis. Figure 11 is a reproduction of the admission roentgenogram.

On the second hospital day 400 c.c. of a serosanguineous fluid (sp. gr. 1.010) containing bile pigments was removed from the left pleural space. A roentgenogram in the left oblique position (Fig.

12) showed the shadow in the right mid-lung field to be definitely triangular in shape and to have the typical appearance of an infarct in the right upper lobe.

On the eighth hospital day 600 c.c. of a similar fluid were removed from the right pleural space. The general condition of the patient was better by the twentieth hospital day; the sputum had diminished to about 30 c.c. daily and was practically free from blood. A roentgenogram at this time (Fig. 13), however, showed an irregular area of diminished density representing an abscess in the previously described infarct.

It was not until the thirty-second hospital day that the sputum became foul and increased to a volume of about 100 c.c. daily. During the next three weeks, with postural drainage, the sputum diminished in amount and became less foul, but remained purulent. A roentgenogram (Fig. 14) at this time no longer showed the abscess cavity. On the sixtieth hospital day the sputum was no longer foul. Five days later the patient was discharged to continue convalescence at home.

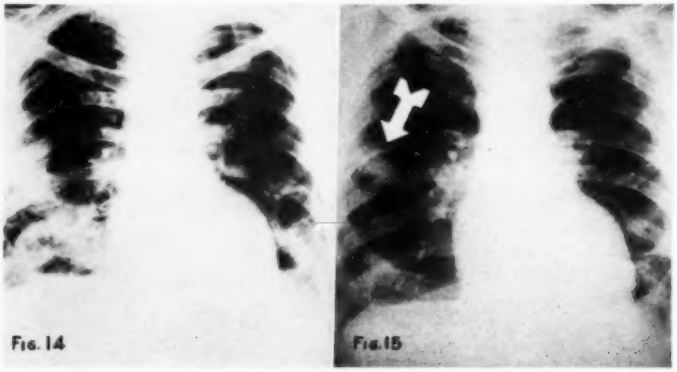
Laboratory work during the hospital stay included five negative blood cultures and four negative pleural fluid cultures. Sputum examination on six occasions failed to reveal tubercle bacilli or pneumococci.

The patient returned for re-examination five weeks later. At that time he had no cardiac failure, no cough, and no sputum. Figure 15 clearly shows the healing of the abscess and the infarct.

Three months later death occurred at home, following a cerebrovascular accident. There was no evidence of recurrent infarction during the terminal illness. Permission for autopsy was not obtained.

Comment: In this case the diagnosis was well established by the classical clinical signs and symptoms and the roentgenologic appearance. The infarct was followed by secondary infection, the roentgenologic demonstration of an abscess cavity, and a foul sputum. The abscess healed, but six months after the infarction, the patient died of a cerebrovascular accident.

CASE 4: T. B., a 66-year-old white male, was admitted to the Medical Service on Nov. 6, 1940, complaining of pain in the left side of the chest of two weeks' duration. He had expectorated a small amount of blood two days before admission. Physical examination revealed a large heart in auricular fibrillation. There was fluid in both pleural spaces in addition to pedal edema.



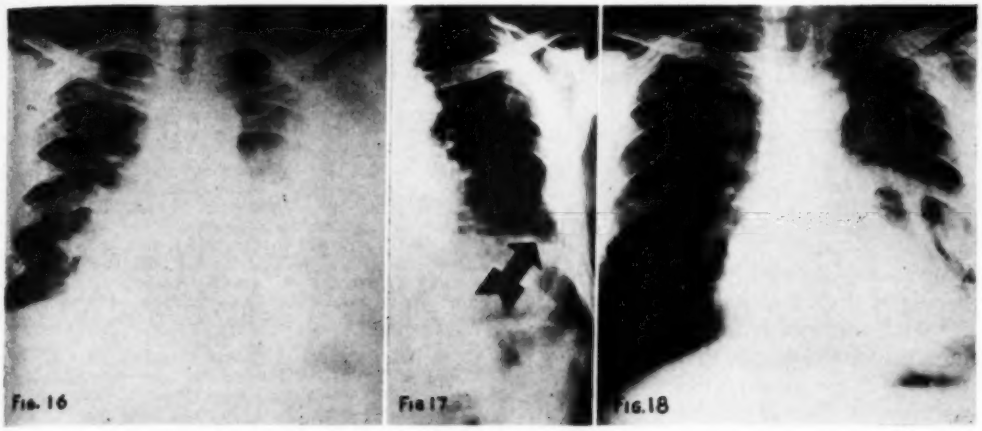
Figs. 14 and 15. Case 3.

Fig. 14. Fifty-seventh hospital day. The pneumothorax space on the left is smaller. The infarct in the right upper lobe is smaller and the abscess cavity is no longer seen. There is still some pleural effusion remaining, and there is much thickening of the pleura in the lower half of the right lung field.

Fig. 15. Five weeks after discharge; 100 days after admission. The area of the infarct is now represented by a scar which has the density and sharpness of fibrous tissue. No passive hyperemia is present. The pneumothorax on the left has disappeared. Some thickened pleura remains at both bases. The patient died three months later following a cerebrovascular accident.

The admission roentgenogram (Fig. 16) revealed a pleural effusion on the left. On the sixth hospital day 950 c.c. of bloody, foul, purulent fluid were removed from the left pleural space in two aspirations and a roentgenogram (Fig. 17) then revealed a fluid level in the left pleural space and an abscess in the lung parenchyma.

The patient was transferred to the Surgical Service and on the tenth hospital day a rib resection and drainage of the empyema pocket were performed. Four days later a pulmono-pleural fistula was dem-



Figs. 16–18. Case 4: Signs and symptoms of infection predominating.

Fig. 16. Second hospital day. Almost the entire left lung field is obscured by a homogeneous shadow of increased density representing a pleural effusion. The cardiac shadow is large, but is in part hidden by the pleural effusion.

Fig. 17. Sixth hospital day. Following two aspirations yielding 950 c.c. of bloody, foul, purulent fluid, a fluid level is seen in the left pleural space. The lung is partially collapsed, but a cavity in the lung parenchyma can be seen (arrow).

Fig. 18. Twenty-sixth hospital day. The empyema has been drained and the lung has almost completely re-expanded. There is much pleural thickening and there is some pleural fluid, but the abscess cavity has closed. The diagnosis of infarct in this case rested on the typical history and course. Following death in cardiac failure some months later, the scar of a healed infarct in the left upper lobe was found.

onstrated by the recovery of methylene blue in the sputum after injection of the dye into the left pleural space. Sixteen days following rib resection the lung had re-expanded and the abscess cavity was no longer visible (Fig. 18).

The postoperative course was uneventful, the cardiac failure disappeared, and the patient was discharged from the hospital.

Six months after discharge death occurred in severe cardiac failure, found at autopsy to be due to arteriolar nephrosclerosis and coronary sclerosis. There were organized thrombi in the branches of the left pulmonary artery, with a stellate scar in the left upper lobe and collapse induration of that lobe. The abscess had healed.

Comment: This case is illustrative of those first seen with the signs and symptoms of infection predominating. The abscess had already formed and was followed by a pulmono-pleural fistula and putrid empyema, with recovery after surgical drainage. An adequate history and the presence of cardiac disease indicated an infarct as the cause of the abscess. This was confirmed postmortem.

SUMMARY AND CONCLUSIONS

In a previously reported study, 344 cases of aseptic hemorrhagic infarcts of the lung were discussed. In 174 of these patients, the infarcts were a significant cause of death. Eleven of these 174 were found at autopsy to have an abscess in the infarct.

Since that time we have been able to make a correct ante-mortem diagnosis of lung abscess complicating pulmonary infarction 6 times in eighteen months. Four of these 6 patients died in the hospital as a result of this complication. Two survived the acute illness, but died in a few months, without recurrence of the infarction.

In the typical case the diagnosis should not be difficult. Hemoptysis will usually herald the onset, accompanied by pain in the chest and followed by leukocytosis and a moderate elevation of temperature. Signs of consolidation and often a pleural friction rub will be found on examination. After an interval of some days or weeks, often when the patient is apparently improving, the sputum increases in amount and becomes foul; a secondary rise in the temperature and leukocyte count occur, and an abscess can be demonstrated roentgenographically. If the patient has

heart disease, the degree of myocardial insufficiency becomes more pronounced. Not infrequently a pulmono-pleural fistula will follow.

The atypical case presents difficulties chiefly because the signs and symptoms of infection, *i.e.*, the abscess, predominate when the patient is first seen. An infarct should be considered as a possible underlying cause in every case of lung abscess, especially if cardiac failure is present.

Roentgenographic findings are especially valuable in the diagnosis of pulmonary infarction if the examinations can be made early in the course of the disease and in several projections. In such cases later development of secondary infection and abscess formation can be clearly seen, and the diagnosis of infarct complicated by abscess formation should be relatively simple. If the abscess is present when the patient is first seen, the signs of the infarct may be hidden, and in such cases the history is of paramount importance.

Four illustrative cases are presented.

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BIBLIOGRAPHY

1. CASTLEMAN, B.: Healed Pulmonary Infarcts. Arch. Path. **30:** 130–142, July 1940.

2. CUTLER, E. C., AND GROSS, R. E.: Nontuberculous Abscess of Lung: Etiology, Treatment, and Results in 90 Cases. J. Thoracic Surg. **6:** 125–155, December 1936.

3. GSELL, O.: Hemorrhagic Lung Infarct and Its Complications. Deutsche med. Wchnschr. **61:** 1317–1320 and 1360–1363, Aug. 16 and 23, 1935.

4. HOLLMANN, W.: Formation of Non-Specific Cavity as a Sequel to Necrotic Softening of Infarct. Deutsche med. Wchnschr. **61:** 906–909, June 7, 1935.

5. KIRKLIN, B. R., AND FAUST, L. S.: A Clinical and Roentgenological Consideration of Pulmonary Infarction, Am. J. Roentgenol. **23:** 265–275, March 1930.

6. KRAUSE, G. R., AND CHESTER, E. M.: Infarction of the Lung: Clinical and Roentgenologic Study. Arch. Int. Med. **67:** 1144–1156, June 1941.

7. LILIENTHAL, H.: Thoracic Surgery. Philadelphia, W. B. Saunders, 1925.

8. LORD, F. T.: Diseases of the Bronchi, Lungs, and Pleura. Philadelphia, Lea & Febiger, 1915.

9. MARKS, J. H.: Pulmonary Infarction as a Cause of Pneumothorax. New England J. Med. **223:** 934–936, Dec. 5, 1940.

10. STEINBERG, I., CLARK, E., AND DE LA CHAPELLE, C.: Suppurative Pleuritis Complicating Pulmonary Infarction in Congestive Heart Failure. Am. J. M. Sc. **194:** 610–617, November 1937.

11. TOUROFF, A. S. W.: Infra-Pulmonary Empyema. Surg., Gynec., & Obst. **57:** 156–169, August 1933.

12. VAN ALLEN, C. M., ADAMS, W. E., AND HRDINA, L. S.: Bronchogenic Contamination in Embolic Abscess of the Lungs. Arch. Surg. **19:** 1262–1278, December 1929. Embolism in Bronchogenic Infection of Lung. Ibid., 1279–1291.

Traumatic Lipo-Hemarthrosis of the Knee[1]

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INJURY TO AND about the knee joint is common in automobile, skiing, and certain industrial accidents. Accuracy in the roentgenographic demonstration and clinical appraisal of the extent of the injury with the least movement of the patient are advisable.

Hemorrhagic fluid is roentgenographically homogeneous. If free fat is present, the fluid is not of homogeneous density, and will tend to separate into layers. Such "fatty" effusion can be taken as an indication of severe injury with tearing of the synovial membrane. A roentgenographic technic which will permit the detection of such separation of a knee-joint effusion into layers and at the same time demand a minimum manipulation of the patient should be of value.

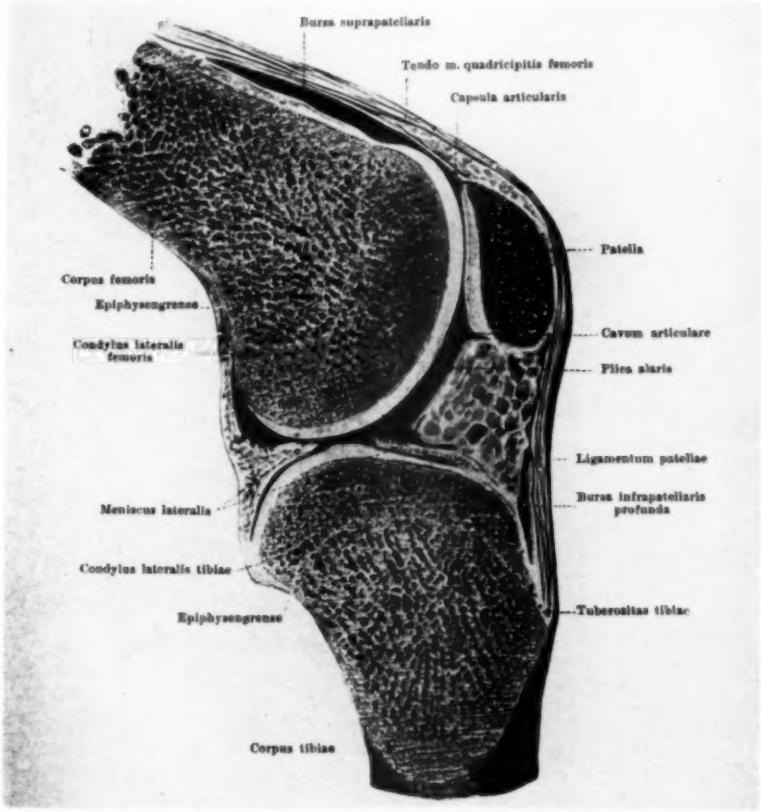

Fig. 1. Sectional view of knee joint (Spalteholz), showing relationship of suprapatellar extension of the synovial sac, the subpatellar fat pad, bursa infrapatellaris profunda and knee joint proper.

The synovial space of the knee joint, partially divided into compartments by

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semilunar cartilage and cruciate ligaments in the adult, commonly communicates with the suprapatellar bursa (Fig. 1), extending upward beneath the tendon of the quadriceps femoris muscle. Inferiorly and anteriorly, it is separated from the patellar ligament and deep infrapatellar bursa by the subpatellar fat (Fig. 2). This highly plastic "subpatellar" fatty mass occupies anterior cruciate ligament. The fat pad and its fringes are within the joint capsule but outside of the synovial membrane. The latter reflects [and enfolds] the plicae alares, and forms a sheath around the plica synovalis" (Kling).

Small collections of fat also lie about the base of the cruciate ligaments and at the back of the joint between the posterior

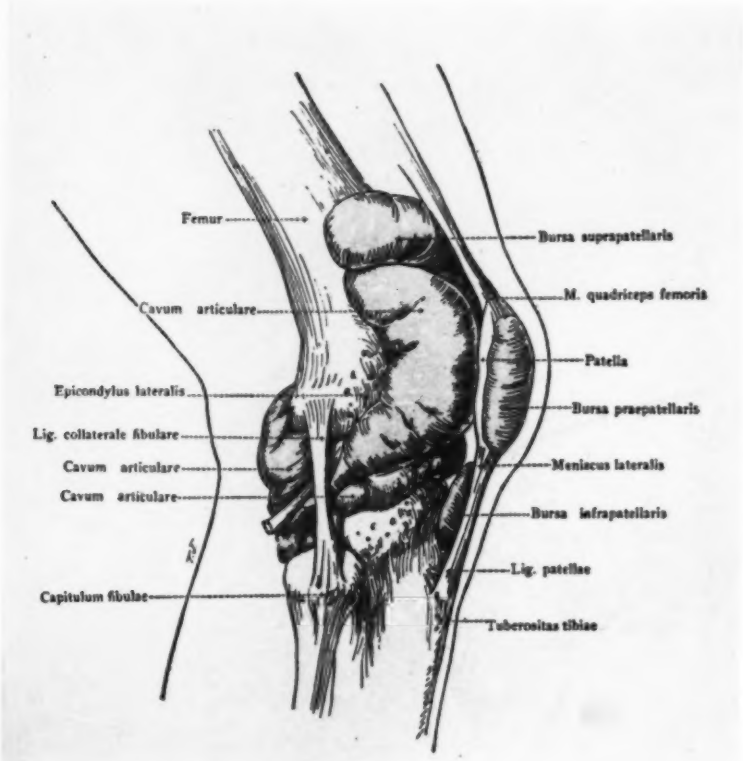

Fig. 2. The bursae about the knee and the synovial sac (cavum articulare) (T. Jones, in *Manual of Surgical Anatomy, U. S. Army*).

a roughly pyramidal space "between the patella [above], the tibia [below], and the patellar ligament [in front] . . . Two triangular fringes [*plicae alares*] project [from it] into the joint cavity from the medial and lateral margins of the patella. They converge in the mid-line and form a narrow band of fat [*plica synovialis patellae*] which crosses the joint cavity and is attached to the [inter-condyloid] notch of the femur in the neighborhood of the cruciate ligament and the capsule. A further deposit of fat, closely neighboring upon the knee joint, varying in degree with age, is to be found in the cancellous bone of the lower end of the femur and the head of the tibia.

None of these deposits of fat lies within the synovial space, nor are other fat deposits in this region likely to become connected with the synovial space in trauma about the knee. Therefore, when fat is pres-

ent in the joint fluid one may assume that there has been severe injury, with the result that the fat has been extravasated from one or more of these depots. In addition, the synovial lining must have been torn.

On the other hand, because of the generous vascular supply about the knee, and the susceptibility of the vascular structure to extravasation of blood as a result of minor injury or in diseases such as cardiorenal or metabolic affections, hemorrhagic effusion may occur without severe trauma. Hemarthrosis of the knee following injury has been reported by Garr, Dickson, and Webb, but with no notation as to the character of the aspirated material save its blood content.

As illustrative examples we present the following seven cases of fracture of the upper tibia, one of which was bilateral. None of these patients presented evidence of infection during observation. In each, fluid levels were observed on the lateral roentgenogram, which had been exposed with the patient supine, the x-ray beam being projected horizontally through the knee joint.

CASE I: H. C. (X-203,073), aged 41 years, male, was admitted Jan. 2, 1940 (Dr. Wilkie), one hour after injury. While he was cranking his motorcycle, his foot had slipped off the pedal, which flew back striking his right knee joint below the patella. There was considerable swelling about the knee, which was fluctuant over the suprapatellar and prepatellar bursae, with marked tenderness over the head of the tibia. No evidence of skin abrasion or puncture wound was found.

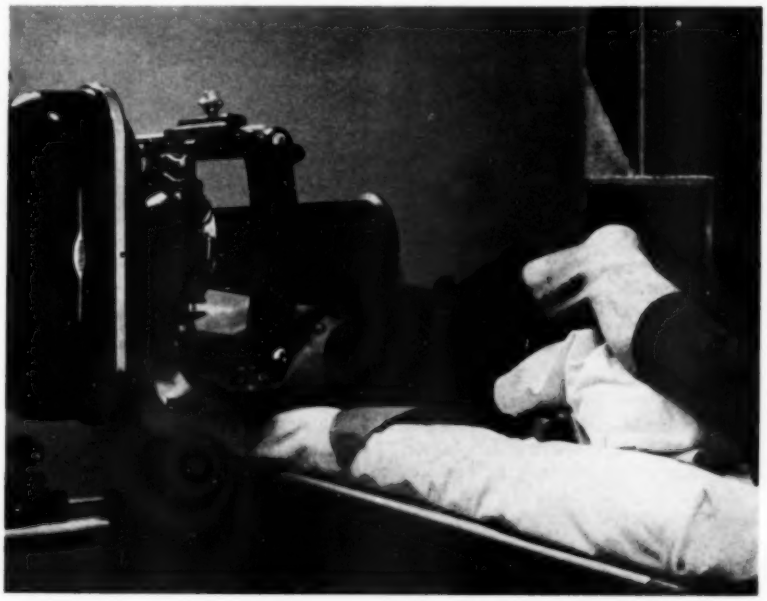

Fig. 3. Position of the patient's knee in relation to the tube and cassette for the horizontal lateral projection, patient supine.

Because of the discomfort incident to turning, the lateral view of the knee was made with the patient supine, the x-ray beam being projected horizontally (Fig. 3). This showed the gross swelling with a fluid level posterior to and extending from 6 cm. above to 5 cm. below the patella; a fracture of the anterior tibial plateau, and a questionable transverse fracture of the tibia 2 cm. below the cruciate spines (Fig. 4). Upon discussion with the attending surgeon (Dr. Wilkie), it was our opinion that, in the absence of any penetrating wound, this appearance must represent fluids of varying specific density.

No aspiration. Uneventful course.

Shortly after observation of this case, one of us (D. C. E.), on reviewing the older files of the Department for teaching material, discovered the following three cases.

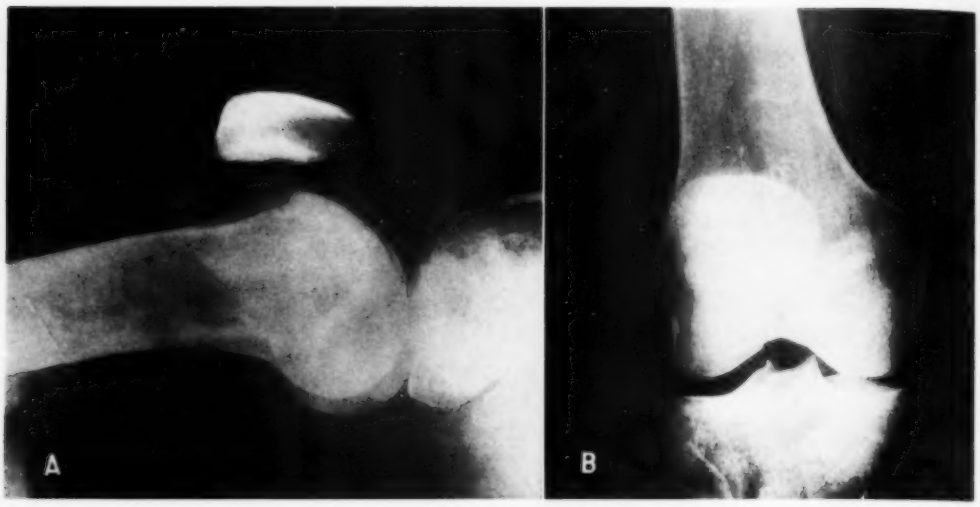

Fig. 4. Case I: Fracture through head of tibia. A. Horizontal lateral projection showing gross fluid separation level in suprapatellar, retropatellar, and infrapatellar spaces; marked contusion of subpatellar fat pad with increased radiolucency, probably due to extravasation of the fat. B. Anteroposterior roentgenogram showing the transverse fracture of the head of tibia.

CASE II: H. L. (X-166,329), aged 32 years, male, was admitted Oct. 23, 1936 (Dr. Wilkie), two hours after being struck by heavy rolls of paper falling on the left leg below the knee. The leg was tensely swollen from the knee to the base of the toes and very tender, with marked deformity in the upper third and increased mobility in every direction. The skin was bruised but unbroken.

Roentgenograms, anteroposterior and lateral supine, showed a comminuted fracture of the upper third of the tibia, becoming intra-articular between the cruciate spines. A fluid level extended above the patella in the upper knee joint and a questionable area of lessened density appeared at the upper end of the distal fragment of the tibia.

Forty-five c.c. of thick blood were aspirated from the joint seven days later. No record was made of other possible content.

CASE III: A. C. (X-175,943), aged 50 years, male, was admitted June 30, 1937 (Dr. G. Miller), shortly after being hit by an automobile, with swelling over the lateral aspect of the lower third of the thigh and marked tenderness posteriorly and laterally in the upper third of the leg. There was a small superficial abrasion of the skin of the knee.

Roentgenograms, anteroposterior and supine, revealed a comminuted vertical fracture of the lateral half of the tibial head involving both cruciate spines, a transverse fracture of the fibula in the upper third, swelling of the anterior soft tissue with a fluid level posterior to the patella extending from 5 cm. above to 1.5 cm. below the patella (Fig. 5).

Not aspirated.

CASE IV: J. S. H. (X-178,418), aged 43, male, was admitted Oct. 1, 1937 (Dr. Keenan), within a few hours after a fall as he was descending from a train. The right leg was swollen and edematous from the knee to the lower third. There was tenderness about the lower part of the patella and upper third of the leg, and the patient was unable to walk. No abrasion or puncture of the skin was noted.

Roentgenograms, anteroposterior and lateral supine, showed a comminuted fracture of the head of the tibia, involving both plateaus, and a possible chip fracture of the lateral femoral condyle. There was a fluid level posterior to the patella from 3 cm. above it to 2 cm. below.

Not aspirated.

In view of these observations, in later cases in which injury about the knee joint was suspected, the routine projection for the lateral roentgenogram was changed to horizontal projection of the x-ray beam, with the patient supine.

Subsequently 3 cases have been observed:

CASE V: J. H. (X-204,382), aged 20, female, was admitted Feb. 18, 1940 (Dr. G. Miller), six hours after a skiing accident. There was marked swelling of the knee joint, with tenderness over the medial side of the knee, but no abrasion of the skin.

Roentgenograms, anteroposterior and lateral supine, showed narrowing of the lateral joint space with relative widening of the mesial joint space, frac-

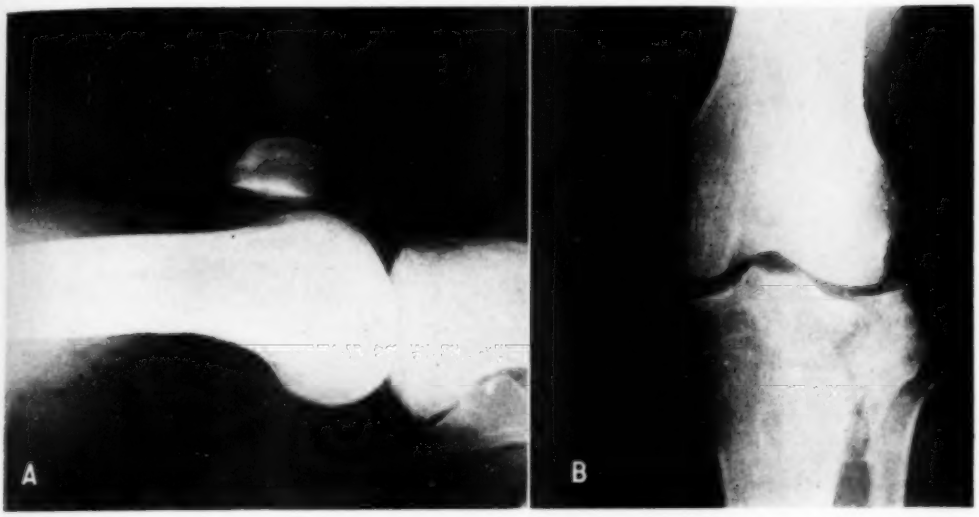

Fig. 5. Case III: Intra-articular fracture of tibia into knee joint. A. Horizontal lateral projection showing fluid separation level in suprapatellar space, extending into infrapatellar space. B. Anteroposterior roentgenogram demonstrating the fracture.

ture of both cruciate spines, swelling of the soft tissue on the medial side. *There were two fluid levels in the anterior soft tissue of the knee, one in line with the posterior surface of the patella and extending above and below the patella for 2 cm.* Slight rotation was present. A probable tear of the medial ligament and damage to the lateral meniscus were suggested (Fig. 6).

Aspiration of the knee was done the day after admission. The fluid withdrawn contained "blood and fatty globules."

In this patient, the bone injury was minimal. The fat was probably extravasated from the several soft tissue depots which we have described above.

CASE VI: S. F. (X-208,534), aged 27, female, was admitted Aug. 16, 1940 (Dr. Armour), shortly after an automobile accident in which she was thrown against the front seat of the car and knocked unconscious. The lower extremities about the knee joints were swollen, reddened, and very painful, and the patient was unable to move her legs. There was no break in the skin of either knee.

Roentgenograms, anteroposterior and lateral supine, revealed on the right a grossly comminuted fracture of the head of the tibia, becoming intra-articular in the mesial plateau and also between the cruciate spines, and a fluid level above the femoral surface of the patella for 2.4 cm.; on the left, a grossly comminuted fracture of the head of the tibia, becoming intra-articular in the lateral plateau, with a fluid level above the femoral surface of the patella for 4 cm., as well as some rarefaction in the region of the subpatellar pad. There was a questionable change in the soft tissue anterior to the tibial tubercle.

Follow-up examination of the right knee, one week later, showed no evidence of residual fluid level, but on the left the fluid level still remained evident two weeks after the injury.

No aspiration.

CASE VII: W. H. (X-52,653), aged 73, male, was admitted Nov. 6, 1940 (Dr. Wilkie), within an hour of being struck on the left knee by an automobile and knocked down. The left knee was swollen and just below it was a small area of ecchymosis. A joint effusion was believed to be present. The skin was intact.

An anteroposterior roentgenogram showed a fracture of the neck of the fibula and a questionable compression fracture of the lateral head of the tibia. A lateral view demonstrated a complete fracture of the tibial head. There was some rarefaction in the region of the subpatellar pad and a fluid level 3 cm. above and posterior to the patella.

Not aspirated.

DISCUSSION

In a review of the literature so far, we have found but one reference to "fluid levels" such as were observed in our cases. That was in a paper by Holmgren of Upsala, Sweden, a copy of which we have not been able to obtain. Nor has that phenomenon been visible upon the roentgenograms used in illustrations of the several pertinent papers.

Walker and Allen described a fracture of the patella with "gas in the joint."

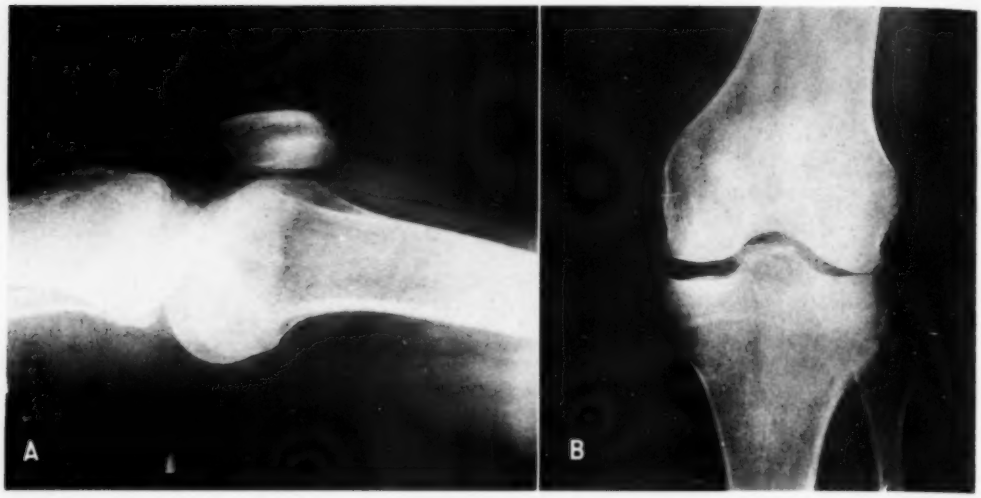

Fig. 6. Case V: Fracture of cruciate spines. A. Horizontal lateral projection demonstrating multiple fluid separation levels in the parapatellar spaces. B. Anteroposterior roentgenogram showing the avulsion fracture of the base of the cruciate spine.

It was believed that the patient had developed a gas bacillus infection *via* a possible puncture wound, 5 mm. long, lateral to the site of fracture. It was also thought that "bubbles" could be expressed from the wound. The culture was negative; temperature, pulse, and respiration were reported as normal throughout, and the patient was subjected to an operative suture of the patella four days after the injury without untoward incident. The roentgenogram made eighteen hours after the injury in this case shows, in the reproduction, an irregular diminished density between the patellar fragments. It is possible that this may indicate extravasation of fat rather than gas as was suspected.

Disorders of the knee joint with supposed injury to the fat depots, with disability but without effusion, have been described by several authors, Annandale (1887), Hoffa (1904), and Guildal. In these cases, bits of the fatty mass have been more or less separated off as loose bodies with varying degrees of fibrosis. To these the name "lipo-arthritis" has been given.

Bissell observed, in one case of fracture of the tibia and fibula, and in two of fracture of the femur, twenty-four to forty-eight hours after injury, a high percentage of fat in the blood (removed from a vein at the elbow).

Kling has called attention to the layering of fluid aspirated from the knee joint in six cases following severe injury. This fluid produced a dependent layer of blood corpuscles, above that a layer of serum, a third of solid neutral fats (palmitin and stearin), and a supernatant layer of liquid fat (olein). Three of the patients had fractures of the tibia or femur, or both.

These several observations, together with that of Phemister, Steen, and Volderauer on the differential density and disposition of liquid fat with other fluid in a closed space (dermoid cyst) have led us to the opinion that the "fluid levels" depicted on our lateral roentgenograms of the knee, made with the patient supine, are the result of extravasation of fat from one or more of the deposits about the joint.

Simple hemorrhage into the joint would produce a roentgenographically homogeneous fluid. Fat would not be emulsified and relatively miscible with the serosanguineous fluid. Therefore, if the fatty deposits contiguous to the knee joint have

been damaged and fat has been extravasated, it would tend to collect, with the patient supine, in the upper portion of the joint, affording a less dense supernatant layer above the serosanguineous effusion.

Positive information as to the presence of fat in the fluid is available in but *one* of our 7 cases. In another, aspiration was done seven days after the injury, but in the record there is only the note that "thick bloody fluid" was removed.

All 8 knees in our 7 cases presented major fluid levels in line with or slightly posterior to the femoral surface of the patella, extending 2 to 5 cm. above the patella, and in 4 (Cases I, III, IV, V) from 1.5 to 5 cm. below the inferior margin of the patella. These were undoubtedly in the synovial space of the knee joint and its connecting suprapatellar bursa. In 2 cases (Cases II and VI) there was some suggestion of extravasation from the tibia into the soft tissue over the anterior surface of the end of the lower fragment.

In 4 instances (II, III, V and VI right) there were gross fractures through the base of the cruciate spines; in 2 (I and V) compressions of the tibial plateau; in 4 (II, III, VI right and left) gross intra-articular vertical fractures of the tibia. It is of interest that none of our patients had sustained a fracture of the femur, the site of major damage being below the patella.

A follow-up observation on Case VI revealed an absence of the fluid level on the right side one week after the injury, whereas on the left side it was still present two weeks after the injury. There had been a greater extent of the fluid level on the left at the initial examination.

CONCLUSIONS

We believe these 8 instances of injury at the knee with fracture of the tibia at the joint and "fluid levels" of differential roentgenographic density present evidence of injury to the fatty tissue collections about the knee joint, particularly the subpatellar fat pad and the base of the cruciate spines. For this syndrome we suggest the designation "traumatic lipohemarthrosis."

The supine position with horizontal projection of the x-ray beam is suggested for the lateral roentgenogram in all cases of suspected injury to the knee joint and upper tibia.

Royal Victoria Hospital
Montreal, Canada

REFERENCES

BISSELL, W. M.: Amount of Fat in the Blood Stream of Persons with Broken Bones. J. A. M. A. **67:** 1926–1927, 1916.

DICKSON, J. A.: Fractures of the Tibia Involving the Knee Joint; "Bumper" or "Fender" Fractures. Am. J. Surg. **38:** 700–705, December 1937.

GARR, C. C.: Traumatic Hemarthrosis of the Knee Joint. South Med. J. **24:** 189–191, March 1931.

GUILDAL, P.: Lipo-arthroitis genus. Acta orthop. Scandinav. **2:** 318–326, 1932.

HOLMGREN, B. S.: Röntgenologisch beobachtete Niveaus zwischen Blut und Fett im Kniegelenk bei intra-artikulärer Fraktur. Upsala läkaref. förh. **45:** 139–142, 1939. Abst. in J. A. M. A., 1940.

KLING, D. H.: Fat in Traumatic Effusions of the Knee Joint. Am. J. Surg. **6:** 71–74, January 1929.

PHEMISTER, D. B., STEEN, W. B., AND VOLDERAUER, J. C.: A Roentgenologic Criterion of Dermoid Cyst. Am. J. Roentgenol. **36:** 14–18, July 1936.

PIERSOL, G. A.: Human Anatomy. Philadelphia, J. B. Lippincott Co., 7th Ed., 1916.

WALKER, M. A., AND ALLEN, LEWIS G.: Air in Knee after Trauma. Radiology **34:** 239, February 1940.

WEBB, R. C.: Fractures of the Upper End of the Tibia Involving the Knee Joint. Minnesota Med. **18:** 186–187, March 1935.

DISCUSSION

Maxwell Harbin, M.D. (Cleveland, Ohio): Unfortunately I have never encountered, or perhaps recognized, the condition in the knee joint described by Doctor Peirce and Doctor Eaglesham, nor have these changes in the x-ray film been seen. I am unable, therefore, to add anything of significance to this discussion of the combination of fat and blood in the knee joint. I am sorry that Doctor Peirce was unable to obtain aspirations in more of these interesting cases, since by so doing he would have obtained much more positive information regarding this situation.

We know, of course, that blood does clot in these knees and the question of relative density may, to a degree, depend upon the clotted blood *versus* the serum. While I have aspirated blood from many traumatized knees, the presence of visible fat globules has not been noticed. It is my understanding that fat and blood were aspirated in only one of Doctor Peirce's seven cases. It would seem, therefore, to be a rather rare occurrence upon the available evidence.

In trauma to the knee it has been my experience that clotting of blood occurs in the joint when there

has been appreciable tearing of synovia or capsule—that is, the tissue-juices favor clotting—whereas in those joints in which hemorrhage is the result of fracture or only slight soft tissue laceration, the blood remains in a liquid state.

Whenever possible, the injured joint should be aspirated under aseptic conditions, since it is well known that free blood in the joint produces damage to the articular cartilage if present over any length of time.

I appreciate very much Dr. Peirce's suggestion referable to the technic of studying these cases, with the patient supine, because, as he has said, it is a painful procedure, many times, to turn the knees to the side. This will, I am sure, be an acceptable technic from the standpoint of the patient.

Carleton B. Peirce, M.D.: I wish particularly to thank Doctor Harbin for his kindly discussion and to state that Doctor Eagleshamand I will be very much pleased to have other observations on this matter. I had hoped that Doctor Harbin might give us some comment as to the character of the subpatellar pad in such cases as may have been seen by him at operation.

Maxwell Harbin, M.D.: As Dr. Peirce has said, there are free fat stores around this particular site, but in my limited experience I have seen no free fat present in joints opened for repair of torn ligaments.

The thing that happens, as a rule, from trauma to the infrapatellar fat pad is hemorrhage. There is quite a blood supply to this fat pad, which is the largest of the fat stores contiguous to and within the joint space. The fat there, in our experience, has never seemed to layer out, or at least we have never seen it as such.

As to the matter of fractures, I think the same might be said so far as our experience goes. I am sorry that I cannot give you more evidence favoring the presence and layering of fat in these joints.

Influence of the Medium on Radiation Injury of Sperm[1]

T. C. EVANS, Ph.D.,[2] J. C. SLAUGHTER, M.A.,[2] E. P. LITTLE, Ph.D.,[3] and G. FAILLA, D.Sc.[4]

EARLY IN THE summer of 1941, Evans and Slaughter (1) found that the fertilizing power of *Arbacia* sperm was reduced by x-irradiation and that the degree of the effect depended largely on the concentration of the sperm suspension in sea water. Sperm irradiated in the seminal fluid with little or no sea water were found to be very resistant to radiation, whereas sperm irradiated in dilute suspension in sea water were quite radiosensitive. Subsequent experiments were designed to throw more light on this interesting phenomenon.

MATERIALS AND METHODS

From the nature of the problem as briefly outlined, it is evident that the experiments involve quantitative determinations. As in all biological problems, the measurement of the "effect" deserves careful consideration. The particular effect of radiation with which we are concerned here is a reduction in the fertilizing power of a sperm suspension. Since all sperm in a suspension are not affected to the same degree by a given dose of radiation, we may think of the radiation effect as a decrease in the number of sperm capable of fertilizing eggs. To measure this accurately it is necessary to determine directly or indirectly the number of sperm which are added to a known number of eggs, and the number of eggs which are fertilized.

Direct counts of the sperm under the conditions of the experiments would be extremely difficult if not impossible. The same purpose, however, can be accomplished, within reasonable limits of accuracy, by the following procedure: Male sea urchins (*Arbacia punctulata*) were stimulated to shed sperm into a dish of sea water, by cutting through the oral region. The suspension was centrifuged until the sperm were closely packed, the supernatant fluid was poured off, and suitable dilutions of the packed sperm were made. With reasonable care in the collection of the sperm and sufficient centrifugation, one may assume that the number of sperm in 1 c.c. of the packed material is essentially the same from one experiment to another. If then the dilutions with sea water are made properly, the *relative* concentrations of sperm in the resultant suspensions are known (and can be relied upon to be substantially constant from one experiment to another). For instance, if 1 c.c. of packed sperm is distributed in 99 c.c. of water, the number of sperm in 1 c.c. of the suspension will be 1 per cent of the number in 1 c.c. of the packed material. Thus, while the absolute number of sperm per unit volume of a given suspension is not known, the number in terms of a reasonably constant standard—centrifugally packed sperm—is known.

Eggs from female urchins were collected in the usual manner. In this case, also, it is not necessary to know the actual number of eggs in a sample, but it is important that all lots used in one experiment have substantially the same number of eggs. As before, a volumetric method was used for this purpose, the suspension being thoroughly stirred before each lot was transferred to an individual dish. (This precaution is necessary because the eggs tend to settle to the bottom rather rapidly.)

Having prepared a sperm suspension of known dilution and egg lots of essentially equal numbers in equal amounts of water, the next step was to determine the minimum volume of the sperm suspension to be added to an egg sample to fertilize all the eggs. This was done by adding drops of sperm suspension in increasing number

[1] From the Marine Biological Laboratory, Woods Hole, Massachusetts. Presented before the Radiological Society of North America, at the Twenty-seventh Annual Meeting, San Francisco, Calif., Dec. 1–5, 1941.

[2] State University of Iowa, Iowa City, Iowa.
[3] Phillips Exeter Academy, Exeter, N. H.
[4] Memorial Hospital, New York, N. Y.

to several egg lots and later observing in which lot slightly less than 100 per cent of the eggs had been fertilized. The counts were usually made at a time sufficiently long after insemination for the eggs to have reached at least the two-cell stage. With the eggs distributed in a single layer at the bottom of the dish, it was a simple matter to count in a given area those which had fertilization membranes and those which had none.

After the sperm suspension had been exposed to x-rays, the same minimum number of drops (as determined above) was added to the egg samples previously prepared. If 50 per cent of the eggs were fertilized it is reasonable to suppose that 50 per cent of the sperm in the suspension were either killed by the radiation or were deprived of their ability to fertilize eggs. This is the criterion of radiation effect used throughout the experiments reported in this paper. The criterion of fertilization of an egg was the presence of the fertilization membrane.

It will be noted that with this procedure the accuracy of the results depends very largely on the addition of the proper number of drops of sperm suspension of known dilution to all the dishes in the experimental set containing substantially the same number of eggs and volume of water. If more than the minimum number of drops required to fertilize just 100 per cent of the eggs in the control lots are added, the effect of the x-ray treatment on the sperm will appear to be less than is actually the case. As a matter of fact, auxiliary tests showed that if a certain number of drops of irradiated sperm suspension fertilized 50 per cent of the eggs, doubling the number of drops produced practically 100 per cent fertilization. With this in view, the minimum number of drops of the control sperm suspension required to fertilize 100 per cent of the eggs in one of the equal lots was always determined experimentally. When sperm suspensions of different dilutions were used in the same experiment, the procedure was to irradiate the sperm at the desired dilutions and then bring all samples to the same dilution, so that the same number of drops could be used for the fertilization determinations.

The method of packing the sperm by centrifugal force before making the desired dilutions was not used in all experiments. At the beginning of the work sperm were collected from the animals in as "dry" a form as possible and the dilutions were based on the volume occupied by the sperm, seminal fluid, and perhaps some water. With this method the results were more variable. In each set of experiments, nevertheless, the results are comparable. In describing the experiments we shall indicate whether the "dry" sperm or "packed" sperm method was used.

The x-ray machine used in these experiments consists of two General Electric XPT water-cooled tubes connected in parallel to a high-tension transformer. Each tube acts as a rectifier and utilizes one-half of the alternating current wave. The tubes are mounted in lead-lined shields with suitable ports to allow the passage of the desired beams of radiation. The material to be irradiated is placed between the two tubes and vertical beams traverse it in opposite directions. With this arrangement the distribution of radiation in the material is more nearly uniform than when only one beam is used. Since the targets of the tubes are water-cooled, there is little heat which can reach the specimen and there is practically no rise in temperature during ordinary treatments. The machine was operated mostly at 182-kv. peak voltage and a current of 25 ma. through each tube. No additional filter was used, the glass wall of the tube being equivalent to a filter of 0.2 mm. copper. The sperm suspension was irradiated in small celluloid containers placed in the center of the field. The depth of the suspension in the containers was kept approximately the same throughout. The intensity of the two x-ray beams together at the point where the specimens were placed was 5,600 roentgens per minute. The desired doses were obtained by vary-

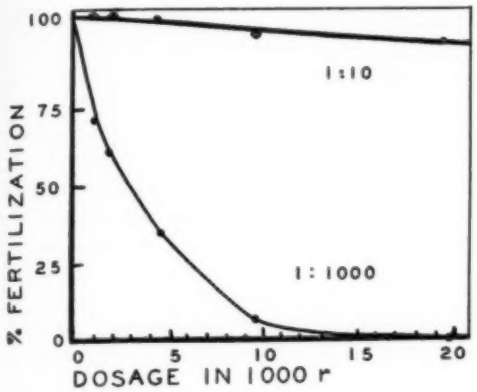

Fig. 1. Effect of roentgen radiation on the fertilizing ability of sperm. Although inseminations with both lots of sperm were done at a concentration of 1:1000, it can be seen that the lot that was irradiated in the concentrated suspension (1 : 10) was much more resistant to the radiation.

ing the time of exposure and timing with a stop watch.

EXPERIMENTAL RESULTS

1. Effect of Sperm Concentration: Sea water dilutions of "dry" sperm were prepared in the ratios of 1:10 and 1:1000. Equal volumes were irradiated simultaneously. The 1:10 suspension was then diluted to 1:1000. Equal numbers of drops of the two 1:1000 suspensions thus obtained were used to inseminate the same number of eggs in different dishes. The results are shown in Figure 1. The great difference in the effect of the radiation is at once apparent. Thus a dose of 10,000 r reduced the fertilizing power of the sperm suspension irradiated at a dilution of 1:1000 to almost zero, whereas it hardly affected the fertilizing power of the sperm suspension irradiated at a dilution of 1:10.

In presenting the experimental results we shall make use at times of the following notation: From a dose-effect curve such as the lower one in Figure 1 (dilution 1:1000), one may determine the dose of radiation which is needed to permit the sperm to fertilize only 50 per cent of the eggs in the sample. We may call this the median effect dose (M.E.D.). The radiation effect under consideration here is that already described, that is, decrease in fertilizing power of the sperm suspension, no matter how it is brought about. From similar curves obtained with sperm irradiated under different conditions, one can obtain the corresponding M.E.D.'s. A large value of the M.E.D. connotes a high "radioresistance" of the sperm suspension and *vice versa*. By taking ratios of the M.E.D.'s a measure of the relative radioresistance of the sperm suspensions irradiated under different conditions is obtained.

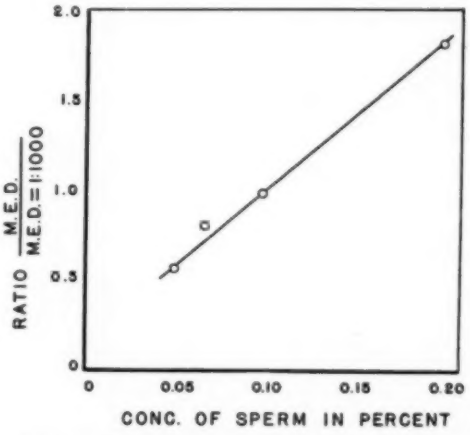

Fig. 2. Results of an experiment in which four suspensions (differing in concentration) of sperm were irradiated. The M.E.D. is the dosage required to reduce the fertilizing capacity of the sperm to fifty per cent.

The results shown in Figure 2 are expressed in these terms. The concentration of sperm in the suspension at the time of irradiation is given in per cent (0.1 per cent concentration corresponds to a dilution of 1:1000). From the figure it will be seen that, as the concentration of sperm increases, the M.E.D., and therefore the radioresistance, increases. Considering the experimental method employed and the paucity of points on the graph, the straight line relation shown in Figure 2 is not really well established. Accordingly, we may conclude that the radioresistance of the sperm suspension increases with the concentration, but the increase is not necessarily proportional to the concentration.

The results just described may be explained on the following basis. A given dose of radiation (*e.g.*, 10,000 r) produces in unit volume of the suspension a definite and limited number of molecules of a "poison" deleterious to the fertilizing power of the sperm. This number of molecules can affect only a certain definite number of sperm, whether one or many molecules are needed for the inactivation of each sperm, provided, of course, that each molecule can react with the sperm only once. Accordingly, 10,000 roentgens can inactivate only a definite number (N) of sperm per cubic centimeter of suspension, no matter how many are present. If the concentration is such that initially there are 2 N active sperm per cubic centimeter, then the radiation will inactivate 50 per cent of the sperm. Similarly, if the suspension contains 4 N active sperm initially, the same dose of radiation will inactivate the same number N, but this is only 25 per cent of the number present per cubic centimeter. It is important to note that subsequent dilution of the irradiated suspension does not alter this ratio. Therefore, after dilution to one quarter, the sperm concentration is N per cubic centimeter, but of these, 75 per cent are capable of fertilizing eggs and 25 per cent are inactive. On the other hand, in the suspension which was irradiated at a concentration of N sperm per cubic centimeter only 50 per cent of the sperm are active. When equal numbers of drops of the two suspensions are used in the fertilization tests, the numbers of fertilized eggs should be in the ratio of 75 to 50. Hence, the sperm suspension irradiated at the higher concentration shows less radiation effect than the suspension irradiated at the lower concentration. This conclusion rests, of course, on the assumption that to inactivate each sperm the same number of molecules of the hypothetical poison are needed, irrespective of the sperm concentration during irradiation.

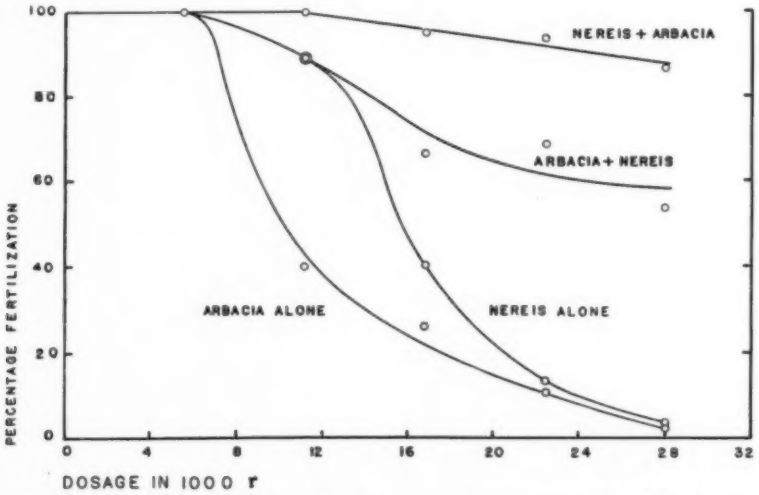

Fig. 3. Results of an experiment in which it was found that the addition of *Nereis* sperm (in a concentration of 1 : 500) to an equal volume of *Arbacia* sperm (1 : 500) increased the resistance over that of either type alone in a concentration of 1 : 1000.

2. Competitive Action of Sperm: Having found that the radiosensitivity of a suspension depends on the concentration of sperm in the case of *Arbacia*, it was of interest to see whether a similar effect could be obtained with another test object. *Nereis* sperm were tried and the results were positive. It became possible then to perform the following experiment: From these two kinds of sperm three sus-

pensions were made: (1) equal volumes of 1:500 *Arbacia* and 1:500 *Nereis* sperm were mixed to give a concentration of either kind of sperm *per se* of 1:1000; (2) the 1:500 *Arbacia* suspension was added to an equal volume of sea water, and (3) the 1:500 *Nereis* suspension was likewise diluted to a final concentration of 1:1000. The three samples were irradiated simultaneously, with the results shown in Figure 3. The curve marked "*Nereis* + *Arbacia*" refers to the determinations in which sperm irradiated in the suspension in the mixture "competed" with the *Arbacia* sperm for the limited number of deleterious units produced in the suspension, and *vice versa*. The experiments from which the curves of Figure 3 are derived were of an exploratory nature, and it is not possible to say whether the two kinds of sperm competed on equal terms for the hypothetical deleterious substance. This problem deserves further study.

3. Protective Action of Various Substances. (*a*) *Seminal Fluid:* From the method of collecting "dry" sperm previously described, it is evident that much of the seminal fluid was present in the samples which were irradiated at the highest concentration and proportionately so for other concentrations. After the "packing" method had been developed, it became possible to determine what part the presence of the seminal fluid played in the radiation effect manifested by the sperm. A large quantity of "dry" sperm was collected and centrifuged without the addition of water. The supernatant liquid, consisting largely of seminal fluid, was then used to make a 1:1000 sperm suspension prepared by the "packing" method. Irra-

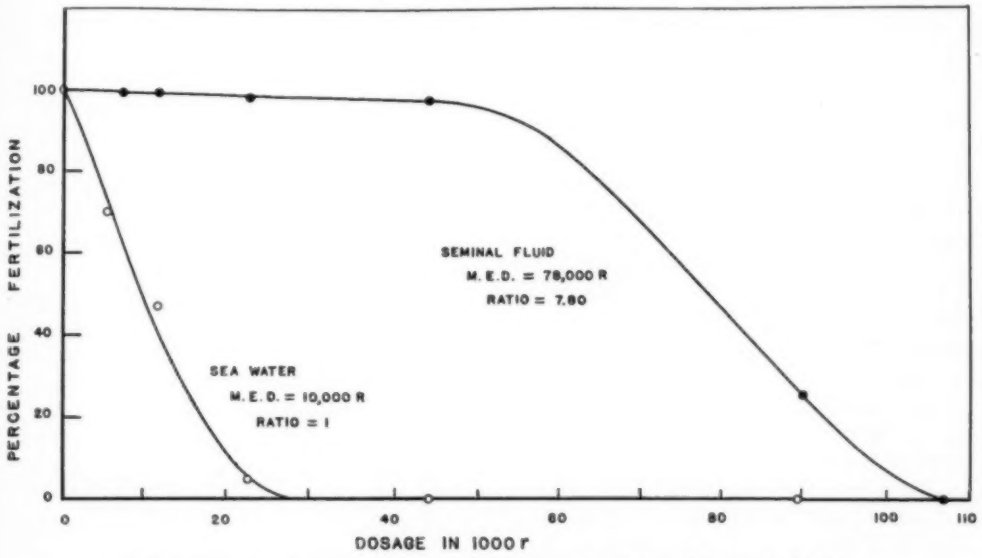

Fig. 4. Results of an experiment indicating protective action of the seminal fluid.

containing both *Arbacia* and *Nereis* sperm were added to *Nereis* eggs. With this information, the notations on the other curves are self-explanatory.

It is plainly evident from the curves that the radiation effect on the two kinds of sperm irradiated in the same suspension was much less than when either kind was in a separate suspension. On the supposition that a certain dose of radiation produces in a given volume of suspension a definite amount of "poison," this shows that the two kinds of sperm irradiated in the same suspension shared the available poison. In other words, the *Nereis* sperm

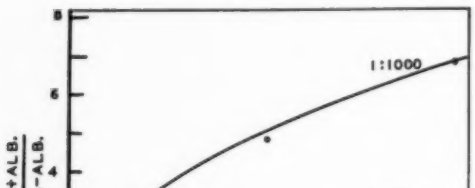

Fig. 5. Relation between the concentration of egg albumin and its protective power. The concentration of sperm during irradiation is indicated on each curve.

diation of this suspension and its appropriate control gave the results shown in Figure 4. The addition of the seminal fluid increased the radioresistance of the sperm suspension 7.8 fold.

In order to retain the poison hypothesis, we must now assume that the deleterious agent is counteracted by one or more of the chemical constituents of seminal fluid. We may then say that something in the seminal fluid competes with the sperm for the "possession" of the available poison molecules in the suspension. As a result, the presence of the seminal fluid *protects* the sperm by "capturing" some of the deleterious products of the radiation.

The results of this experiment suggest some parallel relation between the radiation effect on sperm and on much simpler systems, such as virus and phage. Recent reports by Friedewald and Anderson (2, 3) and Luria and Exner (4) bring out the fact that the radiosensitivity of rabbit papilloma virus or certain bacteriophages increases markedly with increasing dilution of the material before irradiation. These authors[5] also report the protective action of proteins present with the virus or phage at the time of the irradiation. In view of this, the protective action of the seminal fluid may be attributed, at least tentatively, to proteins contained therein. The natural extension of the work was then to introduce different known substances in the sperm suspension, before irradiation.

(*b*) *Egg Albumin:* The protective effect of egg albumin added to the sperm suspension before irradiation is shown in Figure 5. The notations on the curves, 1:1000 and 1:100, refer to the concentrations of the sperm in the suspensions containing also different percentages of egg albumin. As would be expected from the preceding discussion, the same concentration of albumin affords greater relative protection to the more dilute suspension of sperm.

In addition to egg albumin, other substances were tested as to their protective influence on *Arbacia* sperm. For the sake of brevity we shall give the results in terms of the ratio of the median effect dose for the 1:1000 sperm suspension containing the additional protective material, to the M.E.D. for the control suspension without such material. The larger the value of this ratio the greater is the protective action of the material. The ratio for 0.1 per cent egg albumin is 7.

(*c*) *Gelatine:* The ratio defined in the preceding paragraph was found to be 7.4 for 0.1 per cent gelatine.

(*d*) *Gum Arabic:* For 0.1 per cent gum arabic the ratio was found to be 2.

(*e*) *Glycylglycine:* Glycylglycine buffered at *p*H 8.2 was used at a concentration of 0.1 per cent of the stock solution. The ratio was 4.2.

(*f*) *Glycine:* Glycine buffered at *p*H 8.2 in a concentration of 0.1 per cent of the stock solution gave a ratio of 2.

(*g*) *Borate Buffer:* It is of interest to note that a non-nitrogenous buffer—borate—at the same *p*H, 8.2, showed no protective action, the ratio being 1.

In comparing the ratios given above and, therefore, the relative protective power of the substances used, it is important to bear in mind that the numerical values are subject to considerable variation from one experiment to another. This is particu-

[5] The work of Friedewald and Anderson was known to one of the present authors (G. F.) before publication, and served as a general guide in planning some of the experiments.

larly true when sperm (and eggs) from different batches of animals are used from one day to another. The variability of results may be attributed in part to the method of determining the fertilizing power of the sperm (which is only relatively quantitative). To make the results more comparable, all controllable experimental conditions were kept as constant as practicable and the protective materials were tested in groups. Thus the ratios for gelatine, glycylglycine, glycine, and borate buffer were determined by simultaneous experiments.

4. Protective Action of "Egg Water": The jelly which surrounds the *Arbacia* egg can be removed by shaking and centrifuging. The supernatant fluid contains a demonstrable amount of jelly (5) along with other substances. We shall refer to this fluid as "egg water." For the experiments a fresh supply of egg water was obtained from a larger number of eggs collected by a procedure analogous to the "dry sperm" method. Concentrations of egg water are expressed in terms of the supernatant fluid as 100 per cent.[6]

It was found that the presence of egg water in the sperm suspension during the irradiation had a very marked protective action. The results of one set of simultaneous determinations with a 1:1000 sperm suspension are shown in Figure 6. It may be well to add that the sperm concentration of 1:1000 refers to the final mixture which was irradiated. For instance, the suspension with 90 per cent egg water was prepared by taking 9 c.c. of egg water and adding 1 c.c. of a 1:100 sperm suspension. The concentration of sperm in the resultant 10 c.c. of mixture was then 1:1000.

As indicated by the curve in Figure 6, the protective power of "egg water" is striking and increases rapidly with its concentration. The sperm irradiated in 90 per cent egg water were apparently 34 times more resistant than sperm irradiated

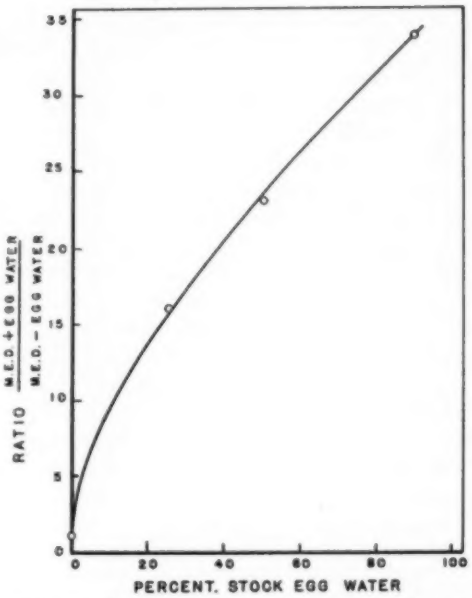

Fig. 6. Relation between the concentration of *Arbacia* egg water and its protective power. The concentration of the sperm during the irradiation was 1 : 1000.

in sea water. In this experiment the median effect dose for the 1:1000 sperm suspension in sea water was 2,000 r, whereas for the corresponding suspension containing 90 per cent egg water it was 68,000 r. In the absence of any definite knowledge as to the chemical composition of egg water, it is impossible to attribute the result to any one constituent. By comparing the curves of Figures 5 and 6 one might surmise that the protective agent in the egg water is able to compete more successfully with *Arbacia* sperm for the possession of the poison molecules previously postulated than egg albumin. Unfortunately we have no data from which we might get a rough estimate of the amount of nitrogenous matter in the egg water. We do know, however, that egg water is present—in various degrees of dilution—when *Arbacia* sperm fertilize eggs in nature, and that it has a powerful physiologic action on the sperm (6). This may have something to do with the results of the experiment. It may be mentioned, also, that the M.E.D. for the 1:1000 sperm

[6] A rough test, made by adding Janus green to a sample of this fluid and centrifuging, showed that the amount of jelly in it was approximately 0.2 per cent.

suspension in sea water varied considerably from day to day. Values in the neighborhood of 2,000 r, as in this experiment, were obtained on several occasions, but usually they ranged from 6,000 to 8,000 r. There may be some connection between the high radiosensitivity of this particular batch of sperm in sea water and the large protective power exhibited by egg water (Fig. 6). In other experiments in which only one (the maximum) concentration of egg water was used the protective ratio was found to be about 12.

5. Loss of Protective Power of Egg Water Induced by X-Rays: If egg water is irradiated before mixing with the sperm suspension, its protective power is reduced. Thus, in one experiment with a 1:1000 sperm suspension, the median effect doses were: for sea water 8,000 r; for egg water 95,000 r; for *irradiated* egg water 62,000 r—the dose previously administered to the egg water having been 151,600 r. This amount of radiation apparently decreased the protective power of the egg water about one-third. It is reasonable to suppose that radiation also influences the protective power of egg water when it is in the sperm suspension and the latter is irradiated. Accordingly, the inherent protective power of egg water is somewhat greater than indicated by the data of Figure 6. In other words, to represent the inherent protective power of egg water, the curve should be steeper. It will be noted in this connection that the dose given the egg water by itself was not very much larger than the M.E.D. for the sperm in the egg water suspension.

6. Direct vs. Indirect Action: The results of experiments described thus far can be accounted for on the basis of the poison hypothesis of Section 1. It is desirable now to consider certain other factors, and particularly some which may provide information concerning the nature of the poison.

The existence of a marked dilution effect indicates that the poison is not produced within the cytoplasm of the sperm. The protective action of various substances leads to the same conclusion. Therefore, according to this hypothesis, radiation acts on the sperm indirectly, that is, by producing a deleterious substance in the medium.

Henshaw (7–10) has studied an effect of x-rays on *Arbacia* sperm which manifests itself as a delay in the time of first cleavage of eggs fertilized with irradiated sperm. In his work sperm were exposed to x-rays in the "dry" form and doses comparable to ours (under the same conditions) were used. Henshaw attributes this effect (cleavage delay) to a direct action of the radiation on the nucleus. If this is correct, one might predict that cleavage delay caused by radiation would not be influenced materially by differences in the medium in which the sperm are irradiated (within the range of media used in our experiments). The results of an experiment planned to test this point are given in Table I. It will be seen that for either dose (5,600 r or 11,200 r) administered to sperm in 1:1000 concentration in different media, the per cent cleavage delay is essentially the same. On the other hand, taking fertilizing power as the criterion of radiation effect, the degree of damage was influenced by the nature of the medium.

TABLE I: EFFECT OF RADIATION ON CLEAVAGE DELAY AS COMPARED TO EFFECT ON PER CENT FERTILIZATION

(Sperm Suspension 1:1000)

Medium	Cleavage Delay		Fertilization
			Ratio: M.E.D. in Test Medium
	5,600 r	11,200 r	M.E.D. in Sea Water
Sea water	72%	120%	1.0
Stock egg water, 100%	70%	120%	11
Stock egg water, 10%	66%	116%	3
Seminal fluid (conc.)	67%	116%	8

Similar results were obtained when the sperm were irradiated at different concentrations. That is, the concentration of the sperm suspension at the time of irradiation had little influence on cleavage

TABLE II: INFLUENCE OF TIME INTERVAL BETWEEN IRRADIATION AND INSEMINATION ON THE PERCENTAGE OF EGGS FERTILIZED BY SPERM IRRADIATED WITH THE SAME DOSE (76,500 R) BUT IN SUSPENSIONS OF DIFFERENT CONCENTRATION

Interval between Irradiation and Insemination	Dry Sperm		1:5 Concentration		1:10 Concentration		1:20 Concentration		1:40 Concentration	
	Control	Irr.	Control	Irr.	Control	Irr.	Control	Irr.	Control	Irr.
75 min.	97%	95%	97%	90%	98%	68%	98%	95%	98%	31%
140 min.	96%	82%	96%	85%	94%	64%	96%	63%	94%	1%
185 min.	93%	98%	92%	88%	93%	76%	98%	58%	95%	1.5%
250 min.	98%	92%	96%	87%	96%	76%	96%	39%	94%	1.3%
310 min.	94%	94%	98%	90%	94%	64%	96%	26%	92%	1.5%

delay. According to the poison hypothesis then, the agent which affects the fertilizing power of the sperm plays little or no part in the cleavage delay reaction.

It is important to note, however, that with the quality of radiation used in the experiments, there cannot be much difference between the amounts of energy absorbed *per unit volume* of the sperm *per se* and of the suspension medium—largely sea water. Hence, there may be, also, a direct action of the radiation on the cytoplasm such as would influence the fertilizing power of the sperm. This would be particularly true in the case of sperm irradiated in high concentration or in the presence of a highly protective material, when the dose required to produce a measurable change is large. Just what part, if any, direct action plays in the reduction of fertilizing power of sperm by radiation cannot be determined from the available experimental data.

7. *Influence of Time:* The reason sufficiently irradiated sperm fail to fertilize eggs is not known. One may suppose that some surface phenomenon is involved, whereby the individual sperm is prevented from entering the egg. On the poison hypothesis, molecules of the deleterious agent, coming in contact with the sperm, might produce the necessary surface change. Now it is well known that chemical changes brought about by x-rays are quantitatively slight. Therefore, the concentration of the hypothetical poison must be extremely weak. If, in addition, a fairly large number of the poison molecules must come in contact with an individual sperm to inactivate it, the element of time comes into the picture. For the same reason the motility of the sperm should play some part in the reaction.

In some experiments designed to test the influence of time, sperm were irradiated in various concentrations and then tested for fertility at different times thereafter. The results of one such experiment are given in Table II. It will be seen that in the more dilute suspensions the radiation effect is greater the longer the interval between irradiation and insemination. In the case of "dry" sperm no radiation effect is evident even after 310 minutes. Presumably, since there is practically no water present in the suspension, there is no poison with which the sperm can come in contact at any time. The 1:5 suspension manifests a slight radiation effect which remains substantially the same throughout the period of observation. In this case one might say that the sperm are able to get all the available poison in a short time. The percentages for the 1:10 suspension are inconsistent with the others. In the case of the 1:20 suspension the radiation effect increases distinctly with time. This is consistent with the poison hypothesis and suggests that, perhaps, many molecules of the poison must come in contact with an individual sperm before its fertilizing power is obliterated.

In another experiment, sperm were irradiated at a concentration of 1:1000 but in two different media and then tested at intervals. Table III shows the results. An increase in radiation effect with time is evident. Also, within ten minutes after the completion of the x-ray treatment one-half of the sperm in the 1:1000 sea water

TABLE III: INFLUENCE OF TIME INTERVAL BETWEEN IRRADIATION AND INSEMINATION ON THE PERCENTAGE OF EGGS FERTILIZED BY SPERM OF THE SAME CONCENTRATION (1:1000) IRRADIATED WITH THE SAME DOSE (8,400 R) BUT IN DIFFERENT MEDIA

Interval between Irradiation and Insemination	Sea Water		Egg Albumin, 0.1 Per Cent	
	Controls	Irr.	Controls	Irr.
10 min.	100%	50%	96%	100%
30 min.	100%	27%	98%	100%
53 min.	100%	16%	100%	94%
93 min.	98%	0%	96%	61%
108 min.	92%	0%	98%	45%
123 min.	82%	0%	92%	18%

suspension were unable to fertilize eggs. This "immediate" effect was always noted in dilute suspensions without protective material. In general, fertilization tests were made as soon as practicable (within a few minutes) after the irradiation and, therefore, the comparative data presented in this paper are for this "immediate" effect of radiation. It is obvious, for instance, from the figures of Table III that the protective ratio of 0.1 per cent egg albumin depends to a considerable extent on the time at which the fertilization tests are made.

The influence of motility of the sperm on the radiation effect was tested in two ways. In the first test advantage was taken of the well known fact that a sperm becomes very active as soon as it is placed in sea water and later swims more slowly. A 1:100 sperm suspension was irradiated immediately after preparation and a second lot twenty-nine minutes later. The radiation effect was much greater in the first specimen.

The other test was carried out as follows. The same amount of sperm in 1:500 concentration in sea water was placed in two identical containers. The sperm in one were packed at the bottom by centrifuging. The two specimens were exposed to x-rays (56,000 r) simultaneously.[7] The radiation effect on the packed sperm was found to be very much less than on the sperm in suspension. At least one difference in the conditions under which the two samples were irradiated was the motility of the sperm, but it would be hazardous to say that the difference in response to radiation was due solely to the difference in motility.

As a matter of fact, the tentative conclusions presented under the heading "Influence of Time" are upset by the following experiment. If the increase in radiation effect with time is due to the gradual acquisition of poison molecules by the sperm over a period of hours (see Table II) the poison must be quite stable. The data of Table II indicate, also, that the presence of water is necessary for the formation of the poison. Non-irradiated sperm placed in irradiated sea water and allowed to remain there for some time in dilute suspension should therefore show a considerable radiation effect. Experiment, however, does not substantiate this expectation. Thus a 1:1000 sperm suspension made with sea water that had just been irradiated with 22,400 r gave practically 100 per cent fertilizations during the first hour; whereas the control suspension, which received the same dose, failed to fertilize eggs even at the first test.[8] It may be supposed that both sperm and sea water must be present during the irradiation in order that the poison may be formed. In the experiment previously described, however, in which the sperm were packed at the bottom of the container, both water and sperm were present during the irradiation (lasting ten minutes), and yet the radiation effect was very much less than in the sample irradiated in suspension, even when the packed sperm were dispersed in the sea water by agitating the container immediately after treatment. Conceivably the poison (or perhaps "latent injury") might be formed in the sperm but not manifest itself unless sufficient water is available. Experiment shows, however, that this is not the case.

A dose of 76,500 r was administered to sperm in the dry form. Sea water dilu-

[7] It should be noted that with the "cross-fire" method of irradiation used in all these experiments, the amount of radiation received by the sperm packed at the bottom of the container and the sperm in suspension in the other container was substantially the same.

[8] Other experiments bearing on this point will be described later.

TABLE IV: INFLUENCE OF TIME INTERVAL BETWEEN DILUTION AND INSEMINATION ON THE PERCENTAGE OF EGGS FERTILIZED WHEN SPERM ARE IRRADIATED (DOSE 76,500 R) "DRY" AND SUBSEQUENTLY DILUTED

Interval between Dilution and Insemination	Sperm Concentration after Irradiation					
	Dry		1:10		1:100	
	Control	Irr.	Control	Irr.	Control	Irr.
35 min.	100%	95%	89%	99%	98%	89%
65 min.	97%	97%	97%	99%	100%	96%
125 min.	100%	100%	98%	98%	100%	100%
245 min.	...	...	92%	98%	100%	96%
365 min.	...	...	100%	98%	100%	100%

tions of 1:10 and 1:100 were then made as soon as possible and kept at 25° C. Fertilization tests were made at different times, and the results are given in Table IV. Evidently dilution after treatment exerts no influence on the radiation effect when the sperm are irradiated "dry." An additional experiment shows that further dilution has no effect when the sperm are irradiated in a 1:20 suspension. Furthermore, the addition of protective material subsequent to the irradiation of the sperm does not influence (counteract) the radiation effect. Accordingly, the indirect effect of radiation on sperm occurs very largely, if not entirely, during the time of treatment. From this it may be concluded that, if radiation produces a poison in the sperm suspension, it must be short-lived. The maximum radiation effect[9] is obtained apparently when, *during the x-ray treatment, the sperm are actively swimming* in a large excess of sea water with no extraneous matter present. The subsequent increase in radiation injury cannot be attributed to a continued action of the poison. (See, however, Section 9.)

In this connection it may be pointed out that, in general, radiobiological effects exhibit a considerable latent period. That is, a certain time elapses between the administration of the radiation and the manifestation of the injury. This interval depends on the type of injury under consideration and, among other factors, on the magnitude of the radiation dose. Thus, to kill a certain organism in a short time, a large dose is required, whereas a much smaller dose will accomplish the same purpose in a longer time. In the latter case, relatively mild interference with vital processes eventually results in death. Perhaps a similar phenomenon is involved in the present case. According to this view, then, the sperm suspension manifests an enhanced radiation effect—that is, more sperm become incapable of fertilizing eggs—with lapse of time, because of biological processes which develop gradually.

8. Influence of Physiological Activity of Sperm: Mention has already been made of the fact that sperm become very active when first placed in sea water and that at this time they are very radiosensitive. It is possible, therefore, that there might be a close correlation between physiological activity and radiosensitivity, such as would account for the results of the experiments reported in this paper. In other words, the dilution effect might be attributed to increased activity of the sperm in the more dilute suspensions; and the protective effect might be due to a decreased activity brought about by the protective substance. Since rate of oxygen consumption is a good index of physiological activity, respiration determinations were made of sperm under different conditions.

The determinations were made in microdifferential respirometers (sensitivity about 0.2 $mm.^3$ O_2) at 25° C. One cubic centimeter of sperm suspension was placed in the experimental cup (volume 5 c.c.) of each respirometer, and 1 c.c. of sea water alone was added to the compensating cup. CO_2 was absorbed by 0.2 c.c. of 10 per cent KOH in the center well of each cup. The respirometers were shaken (5.5 cm. ex-

[9] Of the type with which we are concerned here.

TABLE V: RESPIRATION OF (NON-IRRADIATED) SPERM IN 1:1000 SUSPENSION IN SEA WATER AND DIFFERENT CONCENTRATIONS OF "EGG WATER"

Interval between Dilution and Respiration Test	Oxygen Consumption in Cubic Mm. per Hour			
	Sea Water	25% Egg Water	50% Egg Water	90% Egg Water
40 min.	4.4	6.6	7.2	5.8
60 min.	3.7	5.7	6.0	4.6
80 min.	2.6	3.6	4.2	3.8
100 min.	2.4	3.8	4.6	4.5
160 min.	1.6	2.2	3.5	4.1
180 min.	0.9	1.4	2.0	2.7
200 min.	0.8	1.2	2.1	2.6
220 min.	1.3	1.3	2.3	3.2
240 min.	0.7	1.2	2.1	2.8
	Fertility tested at this time. Percentage eggs fertilized			
260 min.	0.5	25	38	61

cursions) 78 times per minute. After an equilibration time of twenty minutes, the respirometers were closed and readings were taken at regular intervals.

Table V shows the results of respiration tests made simultaneously on (non-irradiated) sperm in 1:1000 suspension in sea water and in different concentrations of "egg water." The volume of the sperm suspension in each manometer was 1 c.c., and the oxygen consumption quite low. This makes the experimental error large, but no better means was available at the time for testing the respiration of sperm in 1:1000 dilutions.[10] The important point which this experiment brings out is the relatively high rate of oxygen consumption of the sperm in the egg water suspensions. Yet it will be recalled that sperm irradiated in egg water are very radioresistant (see Fig. 6). We must conclude, therefore, that sperm which are physiologically very active are not necessarily radiosensitive.

Fertility tests of the sperm in the manometers were made at the 260-minute period, and the results are given at the bottom of the table. They show that the sperm in the egg water suspensions not only consume more oxygen but they are better able to fertilize eggs four hours and twenty minutes after the 1:1000 suspensions were prepared. The egg water, therefore, protects the sperm from radiation damage and apparently from—shall we say?—"natural wear and tear."

Respiration tests of sperm in different sea water dilutions show that the greater the dilution the greater the oxygen consumption per sperm and the shorter the period during which the sperm are still capable of fertilizing eggs. The respiration of packed sperm is practically nil but the "life" very long. In the case of sperm in 1:1000 concentration in sea water the respiration rate (per individual) is high but the life short—about four hours. One might say, therefore, that radiation accelerates a natural process and causes the sperm to die sooner; whereas the protective material retards the same process and consequently the suspension contains more viable sperm at any given time than it would have otherwise, whether or not it had been irradiated. If this is the case, the protective substance does not really protect the sperm. Just as many may be inactivated by the radiation, but many may have had their life prolonged by the protective material, and the observed result is an apparent protection against radiation injury.

Whether this explanation is valid or not could be determined by counting the sperm and eggs used in the fertilization tests. In the first place, it cannot be correct unless the number of sperm added to the egg suspension is very much larger than the number of eggs present. This we do not know by actual count, but we do know that only enough sperm were added to get just 100 per cent of the eggs in the controls fertilized. No doubt under these conditions there is an excess of sperm over the number of eggs, but how large an excess we do not know. It is unlikely, however, that it is large enough to account (on the prolongation of life hypothesis) for the high protective power exhibited by some of the substances used in the experiments. This explanation is rendered even less probable by the following experiment.

[10] It was thought important to use a high dilution because of the fact that the protective effect is great under these conditions. Other similar tests with more concentrated sperm (1 drop in 9 drops of suspension medium) confirm these findings.

Five lots of 1:1000 sperm suspension were prepared. The first was a suspension in sea water which was given a dose of 8,400 r; the second an identical suspension which was not irradiated and served as control. The third was a suspension in sea water containing 0.1 per cent egg albumin, which was irradiated simultaneously with No. 1 and received a dose of 8,400 r; the fourth an identical suspension in sea water containing 0.1 per cent egg albumin which served as control for No. 3. The fifth was a suspension in sea water which was irradiated simultaneously with No. 1 and No. 3 and received a dose of 8,400 r. Immediately following the x-ray treatment, egg albumin was added to this lot so as to bring its concentration in the suspension to 0.1 per cent. This increased somewhat the volume of the sample and, therefore, at this time the volumes of the other four were increased to the same extent by adding equal amounts of sea water. Reckoning time from the moment that the 1:1000 sperm suspensions were prepared, the x-ray treatment (lasting one and a half minutes) was given twenty-two minutes later; the first inseminations for the fertilization tests were made nine minutes after the end of the treatment. Other fertilization tests were made subsequently as shown by the experimental points in Figure 7. The two lowest curves are of chief interest for the present purpose. They show that when sperm in 1:1000 concentration is irradiated in sea water alone, addition of 0.1 per cent egg albumin immediately after treatment does not alter the radiation effect. On the other hand, the same concentration of egg albumin present during the irradiation does diminish the radiation effect markedly, as shown by the middle curve in the figure.

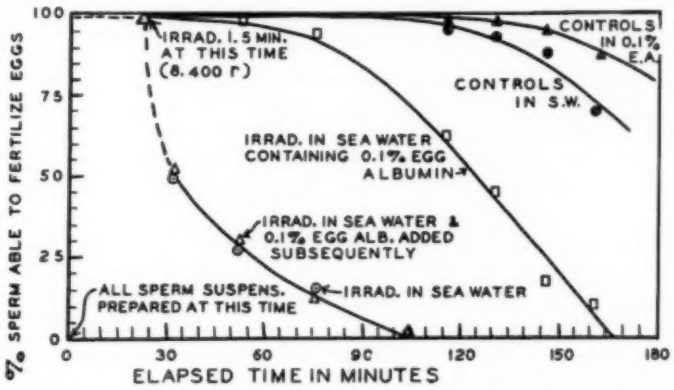

Fig. 7. Survival of sperm in 1 : 1000 concentration with respect to time, under different conditions.

9. Nature of the "Poison": We have shown that, at least qualitatively, most of the experimental results presented so far can be accounted for on the basis of the poison hypothesis, provided the poison is short-lived. Now it is known that x-rays produce hydrogen peroxide in water (11–15), albeit in minute concentration. Owing to the presence of organic matter in the sperm suspensions (and sea water itself), the life of the hydrogen peroxide produced therein might well be very short. It is also known that sperm in general are killed readily by very low concentrations of hydrogen peroxide. Furthermore, numerical calculations based on data available in the literature (13, 14), show that the concentration of hydrogen peroxide which may be expected to be produced by x-ray doses such as we used is approximately of the same order of magnitude (1:1,000,000) as that known to be lethal to

some sperm. It is of interest, therefore, to determine whether the radiation effect under consideration can be attributed to hydrogen peroxide.

Addition of titanic chloride to heavily irradiated sea water revealed the presence of hydrogen peroxide by a faint but definite color change. Samples of sea water were then irradiated with doses of 56,000 to 336,000 r. Other samples in identical containers were prepared in which hydrogen peroxide[11] was present in different concentrations down to 1:10,000,000. Titanic chloride was added to all the samples and a Kodachrome photograph was taken with the irradiated and H_2O_2 samples in juxtaposition. Visual comparison of the colorations indicated that (if the color change in the irradiated sea water was due entirely to the presence of hydrogen peroxide) the concentration of H_2O_2 in the sample irradiated with 56,000 r was definitely less than 1:1,000,000, perhaps 1:2,000,000.

The effect of 1:1,000,000 H_2O_2 on sperm in 1:1000 suspension was tested under various conditions. The "survival" curve, C, shown at the lower left of Figure 8 was obtained by making fertilization tests at different times after the hydrogen peroxide had been added to the sperm suspension. It is evident that H_2O_2 in this concentration has a marked deleterious influence on sperm in the 1:1000 suspension. For the purpose at hand, however, it is important to compare this with the radiation effect on the same sperm in 1:1000 suspension. Survival curve A in Figure 8 was obtained with a dose of 16,800 r. The point of chief interest is that the fertilizing power of the irradiated sperm suspension dropped approximately 60 per cent in the three minutes during which the treatment was given. During the same short interval the fertilizing power of sperm in H_2O_2 (curve C) dropped very little. Considering that the concentration of H_2O_2 which could be produced by 16,800 r is much less than 1:1,000,000, it is evident that H_2O_2 in the irradiated suspension had little or nothing to do with the large drop in fertilizing power. We must conclude, therefore, that radiation does not act on the sperm through the intermediary of hydrogen peroxide produced in the suspension.

In Figure 8 are shown, also, other experimental results which tend to support the conclusion that the loss of fertilizing power of an irradiated sperm suspension is not due to hydrogen peroxide. Comparison of curves A and B reveals the great protective action of albumin when present in the sperm suspension during x-ray treatment. The same egg albumin was used in a 1:1000 sperm suspension containing fresh hydrogen peroxide in concentration of 1:1,000,000. The results are shown by curve D. Comparing curves C and D it will be seen that 0.1 per cent egg albumin does not protect sperm from the action of hydrogen peroxide, whereas, as already stated, it protects the same sperm from the action of x-rays (curves A and B). Since this is an important point, numerous experiments were carried out to test it critically, but for some unaccountable reasons the results were not consistent. It is safer to say, therefore, that the protective action of 0.1 per cent egg albumin on sperm in dilute suspension is much less marked when the sperm are subjected to 1:1,000,000 hydrogen peroxide than when they are exposed to x-rays under comparable conditions.

As previously mentioned, it might be expected that very dilute H_2O_2 would decompose rapidly in sea water. Experiment shows that while decomposition does take place, it is not very rapid even in the 1:1,000,000 solution, as indicated by a considerable effect on sperm after standing for ten to forty-five minutes at room temperature.

Now we have seen that H_2O_2 in 1:1,000,000 concentration in due course exerts a deleterious influence on dilute sperm. The titanic chloride test shows that heavily irradiated sea water contains H_2O_2 in concentration of the same order of magnitude.

[11] Merck's Superoxol, reagent hydrogen peroxide 30 per cent.

Also, H_2O_2 in about this concentration does not decompose very rapidly. Therefore, heavily irradiated sea water should injure dilute sperm if allowed to act for a sufficiently long time. This has been confirmed by experiments in which 1:1000 sperm suspensions were made in water previously irradiated with doses of the order of 100,000 r. The effect on the sperm increases with time, as in the case of the sperm suspensions to which H_2O_2 had been added. This result does not contradict the finding reported in Section 7, which was for water irradiated with the relatively small doses needed to inactivate sperm in 1:1000 suspensions. To obtain an effect on the sperm by irradiating the water alone,[12] very much larger doses are necessary.

From the available experimental evidence we may conclude that, even though hydrogen peroxide is formed in sea water by x-rays, the concentration is entirely inadequate to account for the "immediate" radiation injury manifested by sperm, whereby it fails to fertilize an egg soon after x-ray treatment. The experiments which exclude hydrogen peroxide from being at least the principal cause of the radiation injury tend to exclude, also, any other short-lived chemical poison which conceivably might be produced *in the medium*.

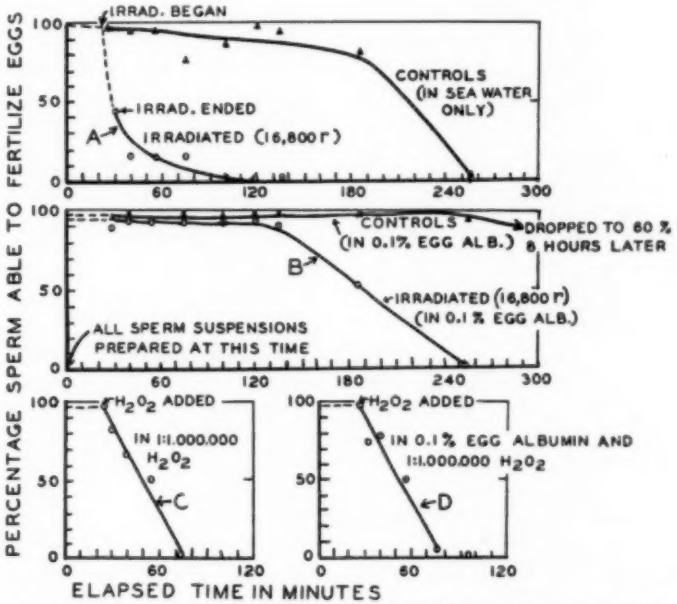

Fig. 8. Survival of sperm in 1 : 1000 concentration with respect to time, under different conditions: A. Irradiated in sea water, 16,800 r. B. Irradiated in sea water containing 0.1 per cent egg albumin, 16,800 r. C. In sea water containing 1 : 1,000,000 H_2O_2. D. In sea water containing 1 : 1,000,000 H_2O_2 and 0.1 per cent egg albumin.

Fricke and his collaborators (12–14) have shown that the action of x-rays on certain chemical compounds irradiated in very low concentrations in water is an indirect one, governed by the absorption of energy by the water rather than by the compound. He has postulated the "activation" of water by the radiation in the sense that a water molecule acquires, temporarily, some energy. This activated water molecule then reacts with a molecule

[12] It may be of interest to mention in passing that dilute sperm kept for some time in heavily irradiated sea water exhibit an appreciable delay in the first and second cleavages of eggs fertilized therewith.

of the chemical compound, causing it to change. Fricke originally suggested this theory to account for the action of radiation on simple inorganic and organic compounds in very dilute solutions. As experimental data have accumulated, it has been found to apply to proteins, such as enzymes (16, 17) and more recently to virus and phage (2–4). It now offers a satisfactory explanation of the bulk of experimental results described in the present paper. It is only necessary to think of the short-lived hypothetical "poison" postulated in the foregoing discussion as consisting of activated water molecules, which Fricke has shown to have an extremely short life. Accordingly, the indirect action of radiation through the intermediary of hypothetic "activated water molecules" has been demonstrated in the case of *living cells*. This is of considerable theoretical interest, but the peculiar conditions under which it takes place should be borne in mind. In the first place, the cells are relatively small and highly motile in dilute suspensions. The nature of the injury inflicted on the sperm is not known, but it may be surmised that a surface phenomenon is involved, and in some way the sperm are prevented from fertilizing eggs. It is important to note that in another effect of radiation on sperm—that responsible for cleavage delay—indirect action plays little or no part. The sum total of the damage to the fertilizing power of sperm manifested at different times, and under different conditions, undoubtedly involves more complex reactions than the initial one brought about by the activated water molecules.

SUMMARIZING REMARKS

X-rays reduce the fertilizing power of a sperm suspension (of *Arbacia punctulata*) in the sense that a certain volume of the irradiated suspension is able to fertilize fewer eggs at a given time than the same volume of the control suspension. Whatever the nature of the change which prevents the sperm from fertilizing an egg may be, it is a definite radiation effect which can be detected immediately after x-ray treatment. With increasing dosage, fewer sperm in a suspension are able to fertilize eggs. Similarly, with lapse of time after the completion of treatment, there is a diminution in the number of sperm capable of fertilizing eggs. The degree of radiation damage to a sperm suspension, however, is greatly influenced by the nature of the medium in which the sperm are in suspension *during the x-ray treatment*.

The influence of several modifications of the medium has been investigated. Obviously, it was necessary to use a quantitative method. One reasonably satisfactory for the purpose at hand was worked out, but it should be borne in mind that it is only relatively quantitative, especially when different lots of sperm and eggs from day to day are involved. The differences in results obtained by changes in the medium are, in general, so large that there can be no doubt of their existence. The actual numerical values probably involve a considerable experimental error. It should be noted, also, that, unless otherwise stated, the fertilizing power of a sperm suspension was determined by insemination tests soon after completion of the x-ray treatment (usually within a few minutes). Since treatments were of short duration, we are dealing in such cases with an "immediate" radiation effect.

Influence of Dilution: The same dose of x-rays administered to sperm in concentrated form and to sea water suspensions containing less and less sperm inactivates an increasingly larger *percentage* of the sperm the more dilute is the suspension. It appears as if a certain dose of radiation inactivates a certain (relatively small) number of sperm in all suspensions. In the very concentrated suspensions this number of damaged sperm is extremely small in comparison with the very large number of sperm present. Accordingly, the percentage change is so small that it may not even be detectable. In very dilute suspensions (1:1000 or less), in which the number of sperm present in the

sample is small, the percentage change is large. In fact, a dose of the order of a few thousand roentgens may be sufficient to inactivate all the sperm.

The influence of dilution was found also in the case of the sperm of the marine worm *Nereis*. Then an interesting corollary was tested experimentally. It was found that the presence of *Nereis* sperm in an *Arbacia* sperm suspension (both highly diluted) decreased the percentage of *Arbacia* sperm inactivated by a given dose of x-rays, while at the same time the *Arbacia* sperm had an analogous effect on the inactivation of *Nereis* sperm.

Influence of Substances Added to Sperm Suspensions: Notable decreases in the percentage of sperm inactivated by a given dose of radiation were found in dilute sperm suspensions containing different concentrations of various substances during irradiation. The following substances were found to give positive results in varying degree: seminal fluid, "egg water," egg albumin, gelatine, gum arabic, glycylglycine (buffered at *p*H 8.2), glycine (buffered at *p*H 8.2). A non-nitrogenous buffer, sodium borate, at *p*H 8.2 had no influence. It is of interest to note that both seminal fluid and "egg water" are normally present in the natural environment in which *Arbacia* sperm fertilize eggs.

Mechanism of the Radiation Reaction: Since the presence of one of the substances just mentioned, in a dilute sperm suspension during the x-ray treatment, increases the dose required to inactivate a given percentage of the sperm present, it may be said that such substances "protect" the sperm from radiation injury. Both the dilution effect and the protective effect may be explained by assuming that radiation acts on the sperm indirectly through the intermediary of activated water molecules. The production of activated water molecules of very short life was postulated by Fricke many years ago to account for some chemical effects of x-rays produced in extremely dilute solutions. The mechanism, then, may be visualized as follows. A given dose of radiation produces in a sperm suspension a definite number of activated water molecules per cubic centimeter. One or many of these activated water molecules react with an individual sperm, causing changes which prevent it from fertilizing an egg. A given number of activated water molecules can influence only a certain number of sperm, which accounts for the dilution effect. If in the suspension are present molecules of substances which can "rob" the activated water molecule of its energy, fewer activated water molecules will act on the sperm. This explains the protective effect. The short life of the activated water molecule accounts for the fact that the protective material must be present in the sperm suspension during the time that it is irradiated. There are, however, complicating factors. Thus, the physiological status of the sperm is altered by dilution and by the addition of protective material. Then in a living cell, reactions initiated by radiation are apt to go on and cause increasingly greater interference with normal physiological processes. In so far as our data permit, some of these factors are discussed in the body of the paper.

Influence of Hydrogen Peroxide: Since the production of hydrogen peroxide in irradiated water is to be expected, and this substance is toxic to sperm, it is important to determine what part it may play in the inactivation of sperm. Our results show that hydrogen peroxide had little or no influence on the "immediate" radiation effect manifested by the sperm (inhibition of fertilizing ability). On the other hand, something that behaves like (and probably is) hydrogen peroxide is produced in sea water in detectable concentrations by *large* doses of x-rays. Very dilute sperm suspensions made with sea water which had been heavily irradiated manifested a more rapid inactivation of sperm with respect to time than the control suspensions. In this connection it should be noted that a gradual decrease in the fertilizing power of sperm occurs normally, but it becomes much more marked the more dilute the suspension. Radiation

(as well as hydrogen peroxide) accelerates this, while protective substances retard it. The phenomenon is very complex and deserves further study.

Cleavage Delay: With increasing dosage, more and more of the sperm in a suspension are inactivated by irradiation. This is true in concentrated suspensions as well as in dilute ones. The difference is that to inactivate a given percentage of the sperm a much larger dose is required in the case of the concentrated suspensions. In any case, therefore, some sperm which have received a considerable dose of radiation remain capable of fertilizing eggs. Henshaw has shown that eggs fertilized with heavily irradiated sperm (in the "dry" form) divide after a longer interval than the controls. We have found that sperm which survive treatment in dilute suspensions, with or without added protective material, cause cleavage delay in the eggs they fertilize, but, of course, to a lesser extent, because of the smaller dose of radiation they can survive. The magnitude of the cleavage delay depends, however, on the dose of radiation received by the sperm and not[13] on the nature of the suspension medium in which they were irradiated (within the limits of our experiments).

Direct and Indirect Action of Radiation: The radiation effect on the sperm which causes cleavage delay in eggs fertilized therewith may be attributed to a direct action of the radiation on the sperm themselves. On the other hand, the effect which inhibits the fertilizing power of sperm[14] is caused largely—according to the evidence presented in this paper—by a special kind of indirect action of radiation, that is, one in which the radiation exerts its influence on the medium of the sperm suspension, producing therein something which then reacts with the sperm. We have, therefore, a striking demonstration of the difference in the mode of action of radiation on the same biological object, depending on the effect which is taken as a criterion of radiation damage.

[13] See, however, footnote 12.

[14] Whether by killing the sperm or otherwise.

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REFERENCES

1. EVANS, T. C., AND SLAUGHTER, J. C.: Effect of Sea Water on the Radiosensitivity of Arbacia Sperm. Collecting Net **16:** 101, 1941.

2. FRIEDEWALD, W. F., AND ANDERSON, R. S.: Factors Influencing the Inactivation of the Rabbit Papilloma Virus by X-rays. Proc. Soc. Exper. Biol. & Med. **45:** 713–715, 1940.

3. FRIEDEWALD, W. F., AND ANDERSON, R. S.: Influence of Extraneous Protein and Virus Concentration on the Inactivation of the Rabbit Papilloma Virus by X-rays. J. Exper. Med. **74:** 463–487, 1941.

4. LURIA, S. E., AND EXNER, FRANK M.: Inactivation of Bacteriophages by X-rays—Influence of the Medium. Proc. Nat. Acad. Sc. **27:** 370–375, 1941.

5. EVANS, T. C., BEAMS, H. W., AND SMITH, M. E.: Effects of Roentgen Radiation on the Jelly of the Arbacia Egg. Biol. Bull. **80:** 363–370, 1941.

6. TYLER, A., AND FOX, S. W.: Evidence for the Protein Nature of the Sperm Agglutinins of the Keyhole Limpet and the Sea-Urchin. Biol. Bull. **79:** 153–165, 1940.

7. HENSHAW, P. S.: Studies of the Effect of Roentgen Rays on the Time of the First Cleavage in Some Marine Invertebrate Eggs. I. Recovery from Roentgen-ray Effects in Arbacia Eggs. Am. J. Roentgenol. **27:** 890–898, 1932.

8. HENSHAW, P. S., AND FRANCIS, D. S.: Effect of X-rays on Cleavage in Arbacia Eggs: Evidence of Nuclear Control of Division Rate. Biol. Bull. **70:** 28–35, 1936.

9. HENSHAW, P. S.: Action of X-rays on Nucleated and Non-Nucleated Egg Fragments. Am. J. Cancer **33:** 258–264, 1938.

10. HENSHAW, P. S.: Further Studies on the Action of Roentgen Rays on the Gametes of Arbacia punctulata. I. Delay in Cell Division Caused by Exposure of Sperm to Roentgen Rays. Am. J. Roentgenol. **43:** 899–906, 1940.

11. RISSE, O.: Die physikalischen Grundlagen der chemischen Wirkungen des Lichts und der Röntgenstrahlen. Ergebn. d. Physiol. **30:** 242–293, 1930.

12. FRICKE, HUGO: The Chemical-Physical Foundation for the Biological Effects of X-rays. Cold Spring Harbor Symp., Quant. Biol. **2:** 241–248, 1934.

13. FRICKE, HUGO: Reduction of Oxygen to Hydrogen Peroxide by the Irradiation of Its Aqueous Solution with X-rays. J. Chem. Physics **2:** 556–557, 1934.

14. FRICKE, HUGO: Chemical Properties of X-ray Activated Molecules with Special Reference to the Water Molecule. Cold Spring Harbor Symp., Quant. Biol. **3:** 55–65, 1935.

15. TAYLOR, C. V., THOMAS, F. O., AND BROWN, M. G.: Studies on Protozoa. IV. Lethal Effects of X-Radiation of a Sterile Culture Medium for "Colpidium compylum." Physiol. Zool. **6:** 467–492, 1933.

16. DALE, W. M.: Effects of X-rays on Enzymes. Biochem. J. **34:** 1367–1373, 1940.

17. TYTELL, A. A., AND KERSTEN, H.: Effects of Soft X-rays on Urease and Catalase. Proc. Soc. Exper. Biol. & Med. **48:** 521–525, 1941.

Roentgenologic Irradiation in Acute Peritonitis and Its Effect on the Cells of Normal Peritoneal Fluid in Guinea-Pigs[1]

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I. ROENTGEN IRRADIATION IN ACUTE PERITONITIS

ROENTGEN irradiation is an accepted method of treating many inflammatory conditions, but its use in acute peritonitis is quite recent and not widespread. Kelly and Dowell advocated roentgen therapy in acute peritonitis and reported 24 cases thus treated.

Literature: Experimental studies of the value of roentgen irradiation in the treatment of acute peritonitis are relatively few. Osugi induced acute diffuse peritonitis in dogs and then irradiated the peritoneal cavity with ultraviolet, infra-red, or roentgen rays. Kelly ligated and punctured the appendixes of dogs. After seven hours in one group and seventeen hours in another, the incisions were opened and it was observed that all the animals had acute spreading peritonitis. The appendix was then removed and roentgen treatment was begun. All irradiations were of 30 r, with the following factors: 85 kv.p., 1 mm. Al filter, 5 ma., and 16 in. (41 cm.) distance. In the first group, the mortality rate among 7 irradiated animals was 14 per cent; in 7 untreated controls it was 43 per cent. In the second group, the mortality rate among 9 irradiated animals was 33 per cent; in 5 untreated animals it was 60 per cent.

Rea reported that radiation therapy in the dosage used by him gave little or no protection to rabbits against peritonitis. He injected 5 c.c. of a peritoneal exudate from a patient dying of peritonitis into the abdomens of rabbits. Six of the rabbits were irradiated with 250 r, the following factors being used: 220 kv.p., 60 cm. distance, and 1 mm. Al filter. Six other animals were not irradiated. Five of the 6 animals receiving roentgen therapy and 4 of the controls died. In another series, 4 rabbits ill with peritonitis all died in spite of irradiation.

Methods: In experiments reported here, peritonitis was induced in male guinea-pigs, seven to eight weeks of age, and weighing between 420 and 450 gm., in different ways. *Escherichia coli* was the organism used to produce the disease because it is the bacterium most frequently found in peritonitis of man and also because it works most satisfactorily in guinea-pigs (Owen). McClure and Altemeier, in 198 cases of acute perforated appendicitis, observed *Escherichia coli* in 77.7 per cent. The next most frequent organism was the non-hemolytic streptococcus, which occurred in 21 per cent of all cases. Owen, working with guinea-pigs, observed that pure cultures of *Escherichia coli*, when given intraperitoneally, produced the most uniform and constant type of peritonitis.

The study reported here confirms much of Owen's work. Peritonitis was produced in guinea-pigs by three different methods. In some the cecum was nicked with scissors; in others a suspension of cecal contents in Ringer's solution was injected intraperitoneally, while in others a broth culture of *Escherichia coli* was injected intraperitoneally. The last method gave the most uniform and virulent type of peritonitis.

Cultures of the organism were maintained throughout the experiment by periodic weekly transfers to a plain agar slant. Prior to inoculation, a small amount of the culture was taken on the end of a platinum wire, transferred to 10 c.c. of plain broth

[1] Work done in the laboratory of Dr. George M. Higgins, Division of Experimental Medicine, Mayo Foundation, Rochester, Minn. Accepted for publication in July 1942.

and incubated for twenty-four hours. One cubic centimeter of the material was then injected intraperitoneally. The peritonitis produced was fairly uniform in type and character. Death, when it occurred, took place on the average within thirteen to sixteen hours. Animals that survived thirty hours did not show any ill effects. Cell counts on the peritoneal fluid obtained by a glass capillary pipet were done on all animals at the time of death, and on a few animals at intervals of two hours prior to death. Air-dried smears of the peritoneal fluid were stained with Gram and with May-Grünwald-Giemsa stains.

Briefly, an inflammatory reaction of the peritoneum, increase in the amount of peritoneal fluid, an influx, within the first twenty-four hours, of heterophilic leukocytes which played a tremendous part in phagocytosing bacteria (Steinberg), early appearance of fibrin, and late appearance of macrophages were common features of the peritonitis observed in all animals.

Seven groups, each composed of 8 animals, were used. All animals in each group received an equal amount of the bacterial solution intraperitoneally, and all were inoculated with the preparation from the same tube of broth. Four in each group received roentgen therapy and 4 did not. The total weight of the 4 treated animals in each group equalled, within 5 to 15 gm., the total weight of the 4 control animals in the group. Roentgen therapy was given, on the average, two and six hours after the intraperitoneal injection. The technical factors were 100 kv.p., 5 ma., 2 mm. Al filter, 20 in. (51 cm.) distance, field 10 × 7 cm., air dose 15 r per minute, half-value layer 3.0 mm. Al. During irradiation a lead shield with an opening 10 cm. long and 7 cm. wide was placed over the animal, with the opening over its abdomen. Since the average thickness of the animal's body was 3.5 cm., the center of the body was estimated to receive 90 per cent of the air dose.

All animals were given two doses of roentgen therapy: one of 40 to 50 r, in air, two hours after the intraperitoneal injection, and a similar dose four hours later. In some groups a total of 85 r was given, and in others 100 r. There was no apparent difference in the results with such small variation of dose.

Results: Of the controls 12, or 42.9 per cent, died of peritonitis; of those receiving roentgen therapy 8, or 28.6 per cent, died. In the animals that died, the average length of life following the intraperitoneal injection was 11.2 hours for the controls and 10.4 hours for the irradiated animals. No significant differences, either in the total peritoneal cell count or in the differential count, were observed between the irradiated and the control groups. The mortality figures of the entire group of animals, irradiated and unirradiated, are shown in Table I.

TABLE I: MORTALITY OF GUINEA-PIGS THAT HAD PERITONITIS

Group	Animals	Died	Hours Died after Injection
Control Group: No Roentgen Therapy			
1	4	3	15–19–12
2	4	3	6–10– 9
3	4	3	13–15– 6
4	4	1	10
5	4	0	..
6	4	1	18
7	4	1	12
Total	28	12	11.2 average
Group Receiving Roentgen Therapy			
1	4	2	16–10
2	4	3	9– 7– 6
3	4	0	..
4	4	2	10–10
5	4	1	15
6	4	0	..
7	4	0	..
Total	28	8	10.4 average

This is a small series of cases, and it is difficult to draw any definite conclusions. Under the conditions of this experiment, however, there was a decrease of 14.3 per cent in the mortality rate among animals which received roentgen irradiation, as compared with an identically similar group that did not receive irradiation. This reduction of mortality percentage is of doubtful significance.

II. EFFECT OF ROENTGEN IRRADIATION ON THE CELLS OF NORMAL PERITONEAL FLUID

Changes induced by roentgen irradiation in most of the tissues and organs of the body have been studied repeatedly, but continued studies of the cellular response of normal peritoneal fluid to irradiation have not been reported.

Literature: The normal peritoneal cavity contains a small amount of a clear fluid. Montgomery studied the number of cells in the peritoneal fluid of many laboratory animals and observed wide variations, the count ranging from 500 to 218,000 per cubic millimeter. The following cells occur in normal peritoneal fluid of the guinea-pig: (1) large phagocytic mononuclear cells, (2) lymphocytes, (3) eosinophils, and (4) heterophilic leukocytes. Dixon and Rixford estimated the number of cells in the peritoneal fluid of man as around 2,300 per cubic millimeter of fluid, of which about 45 per cent were macrophages, many were lymphocytes, a few were eosinophils and basophils, but only a small percentage were neutrophils.

Considerable work has been reported on the cellular response of the peritoneal fluid to various substances. The intraperitoneal injection of vaccines, concentrated amniotic fluid, sodium ricinoleate, and other irritating substances induced an increase in the total amount of peritoneal fluid and a rapid increase in the number of leukocytes within the first twenty-four hours and a rise in the number of macrophages over a period of days (Seeley, Higgins and Mann). This reaction parallels that seen in bacterial peritonitis itself.

Rea irradiated the abdomens of 3 rabbits, giving each 250 r at 220 kv.p. After three days the peritoneal fluid revealed only an occasional macrophage and leukocyte. The total cell counts were no greater than those of the three control rabbits. Altemeier and Jones gave 630 r, using 200 kv., approximately 90 per cent of a human erythema dose of roentgen rays, over the entire anterior aspect of the abdominal wall of rabbits. Fluid aspirated from the dependent portion of the abdominal cavity of animals irradiated forty-eight hours previously revealed an increased amount of fluid with numerous erythrocytes and flakes of fibrin, along with the normal cellular components.

The intestinal mucosa is thought to be more sensitive to roentgen rays than the liver. Chrom irradiated the intestines of normal mice with doses up to 1,100 r, without any noticeable effect. Irradiation of the entire abdomen, including the liver and spleen, gave rise to progressive bacteriemia. Histologic studies were interpreted as showing that after irradiation the epithelial cells of the intestine, especially in the ileocecal region, may lose their ability to retain the bacteria normally present in the intestinal lumen. K'o, Tu, and Chan gave, through the abdominal wall, in a protracted course, a total depth dose of 2,400 r to the intestines of dogs fed inorganic compounds of iron. The animals did not show any clinical symptoms during the course of the treatment and pathologic changes in the small intestine did not occur.

Michels studied the omentum of rabbits that had been given intravenous injections of India ink and particles of carbon previous to irradiation with 400 r at 200 kv.p. The animals were killed at ten different intervals up to ninety-six hours after irradiation. There was evidence of lymphoid degeneration, the earliest at five hours and the latest forty-five hours after irradiation. At five to eighteen hours after irradiation, the omental capillaries were engorged with heterophilic leukocytes, a vast number of which had migrated into the tissues, where they disintegrated, presumably liberating a defense substance. Michels expressed the belief that the lymphoid tissue was stimulated to a heightened proliferation at the end of three days. The endothelial cells in the omentum either degenerated or were transformed into fibroblasts. A constant effect of the single irradiation was the production of regions of fibrosis in the omentum. The order of sensitiveness of the omental connective tissue cells was as follows: lymphocytes, pseudo-eosinophilic leukocytes, eosinophils, plasma cells, mono-

cytes, endothelium, pericytes, fat cells, polyblasts or histiocytes, fibrocytes, mesothelial and mast cells.

Mechanism of Effect of Roentgen Irradiation on Inflammation: Before the present investigation and the results obtained are described, a brief review of the mechanisms involved in the roentgen irradiation of inflammation may be useful. These have been considered under four headings by Pendergrass and Hodes. The first is the effect of roentgen irradiation on bacteria. Massive, intensive irradiation, greater than that ever used in human diseases, is bactericidal. At the present time, however, it is agreed that the effect of roentgen irradiation, in doses used for the treatment of inflammation, is not due to a primary effect on the bacteria.

The second mechanism is the effect of roentgen irradiation on the normal cellular response to tissue irritants. Menkin (17, 18), Rich, and others (30, 31) have described clearly the complex nature of the changes that occur during inflammation or irritation. One such prominent change is leukocytic infiltration, which varies in degree and type depending on the nature of the organism or irritant. Numerous experiments have determined definitely that the lymphocyte is the most radiosensitive cell in the human body, showing degenerative changes within half an hour after exposure (Warthin; Taylor, Witherbee, and Murphy). The neutrophilic leukocyte and the eosinophilic leukocyte follow in sensitivity, with degenerative changes becoming perceptible twelve to twenty-four hours after irradiation. Desjardins expressed the belief that the striking effect of irradiation on inflammation is due to the early destruction of the leukocytes, which sets free protective antibodies at the site of inflammation more quickly than normally occurs in the natural course of inflammation. This mechanism is the one most frequently quoted and is most often accepted as the basic effect of roentgen irradiation on inflammation. Pendergrass and Hodes, however, questioned whether the more resistant polymorphonuclear neutrophilic leukocytes are destroyed by doses of 75 to 200 r, the range of dosage commonly used for localized infection.

The third mechanism is the effect on normal immunologic responses (Simonds and Jones; Corper and Chovey; Corper; Hektoen (8, 9); Hektoen and Corper; Kellert; Morton). Most investigators are agreed that the bactericidal quality of blood is enhanced by small doses of radiation. Once formation of antibodies is under way, small doses of radiation seem to have little effect. It is thought that antibodies are specialized globulins that appear in the blood serum or body fluids in response to an irritant with which they react specifically.

The fourth mechanism is the effect on the vascular system. Small doses of radiation uniformly cause dilation of the capillary network and an increase of the rate and quantity of blood flow through the irradiated region. These changes are of the type seen in active hyperemia, and Pendergrass and Hodes expressed the belief that they are of considerable importance in the radiation therapy of infections.

Methods: In the present study, male stock guinea-pigs, seven to eight weeks of age, weighing on the average 420 to 450 gm., were given various doses of roentgen rays. The peritoneal fluid was examined periodically, the total number of cells was counted and stained smears were prepared. The irradiation factors were as follows: 100 kv.p., 5 ma., 2 mm. Al filter, 20 in. (51 cm.) distance, portal 10 × 7 cm., air dose 15 r per minute, half-value layer 3 mm. Al.

For control data three examinations of the cells of the peritoneal exudate were made prior to irradiation, at intervals of two days. Samples of fluid were then obtained at two, six, nine, twelve, and twenty-four hours, two, four, and seven days, and weekly thereafter until the tenth week, then at the twelfth and finally at the fourteenth week. In two groups of animals observations were made up to twenty weeks following irradiation. A total of 1,248 cell counts and differential smears of peritoneal fluid were made.

Varying air doses of roentgen rays up to 1,000 r were given. Nine animals served as controls. Three animals were given 25 r; three, 50 r; nine, 100 r in a single dose; eleven, 100 r in divided doses, that is, 50 r followed in four hours by another 50 r; four, 200 r; five, 400 r; five, a total of 700 r in two doses; and five, a total of 1,000 r in three doses. A cell count was obtained and air-dried smears, stained with May-Grünwald-Giemsa stain, were prepared from every specimen of peritoneal fluid. No attempt was made to determine the total amount of fluid present, since this procedure would have necessitated killing the animal.

Observations were recorded several times during the first twenty-four hours in order to determine the immediate effect induced by irradiation. It was thought that early reactions, if occurring, might be helpful in determining the rationale for irradiation therapy in acute peritonitis. Weekly observations were made for two reasons: (1) to follow the delayed effects of irradiation for a sufficiently long time and (2) to investigate some extremely interesting statements published by Altemeier and Jones. They observed that a group of 42 rabbits receiving doses of 630 r (200 kv.p., 25 ma., and 0.5 mm. Cu plus 1 mm. Al filter) were protected against the intraperitoneal injection of mixed, highly virulent bacterial cultures. The degree of protection rose sharply three weeks after irradiation and reached its maximum between the fourth and the sixth week. At this time 12 of 17 animals (70.6 per cent) that had received irradiation survived a dose of mixed bacteria from a case of fatal peritonitis. In a control group not treated by roentgen rays, all died after a similar injection. From a study of these experiments and a review of the literature, Altemeier and Jones were unable to explain the manner in which this protection was brought about. They did not, however, make any attempt to examine the peritoneal fluid at periodic intervals, and it seemed to us that such studies might throw some light on this problem.

Results: Examination of the peritoneal fluid obtained by a capillary pipet revealed several different types of cells: (1) macrophages, which correspond to the polyblasts of the inflammatory exudate which originate through mobilization of the local histiocytes; (2) desquamated mesothelial cells; (3) lymphocytes; (4) small lymphocytes, containing a large spherical inclusion in the protoplasm, the Kurloff body; (5) eosinophilic leukocytes of hematogenous origin; (6) occasional basophilic leukocytes; finally (7) heterophilic leukocytes (Maximow). The heterophilic leukocytes, not ordinarily found in the normal peritoneal fluid, differ slightly in the guinea-pig from those found in other animals, in that the granules present within their cytoplasm have a slight predilection for acid dyes instead of being neutral, that is, neutrophilic, and are therefore also called pseudo-eosinophilic leukocytes.

The macrophage, as well as the heterophilic leukocyte, possesses the ability to phagocytize bacteria. At the local site of inflammation in previously uninflamed tissue, macrophages do not appear in great numbers until at least twenty-four—more frequently forty-eight—hours have elapsed. They arise through mobilization of local histiocytes and lymphocytes. The heterophilic leukocytes, on the other hand, are brought to the site of injury *via* the blood stream and arrive in large numbers within the first twenty-four hours. Steinberg and Martin concluded that macrophages appear, not as a response to bacterial invasion *per se*, but rather as a result of the action of the heterophils.

The heterophilic leukocytes are the body's first line of defense against invading bacteria. According to Menkin (17), a substance called leukotaxine, present in inflammatory exudate, causes a rapid migration of these cells through the endothelial walls of the small vessels. When they disintegrate in a region of inflammation, they liberate certain proteolytic ferments which have a slight bactericidal power. Constituents of the exudate other than the intact heterophil, however, played

little part in the preservation of life in experiments in which living cells were transferred to animals having an otherwise lethal peritoneal infection (Steinberg).

Menkin (18) stated that the cytologic character of the inflammatory exudate varies, depending on the hydrogen ion concentration. Steinberg and Dietz, however, failed to find any correlation between the hydrogen ion concentration and the cell type, the number of degenerated cells, or the relative number of free or phagocytized bacteria.

The functions of the lymphocyte and of the eosinophilic and the basophilic leukocytes remain fundamentally a mystery. Lymphocytes collect around regions of inflammation, especially those of a chronic nature, but presumably do not engage in phagocytosis. Maximow expressed the belief that the lymphocyte may be one of the sources of the macrophage. Kolouch (quoted by Bell) gave good evidence for this. Eosinophils appear most numerous in certain allergic conditions but little is known definitely regarding their function.

In this series of experiments, as pointed out above, 9 control animals received no irradiation. These were examined at the same time intervals as the irradiated animals. Five of these 9 animals were provided water freely from the beginning of the experiment, but the water supply for the remaining four was restricted. After two weeks, water was again given freely to these four animals, and within twenty-four hours the total peritoneal cell count per cubic millimeter of fluid dropped to a little more than half of what it had been before adequate amounts of water were provided. Similar experiences with another group of animals demonstrated that a reduced intake of water induced a relative increase in the number of cells per cubic millimeter of fluid, whereas increased consumption of water caused a rapid diminution of the concentration of cells per unit volume.

In the group of 5 animals that were provided water freely the number of cells per cubic millimeter of peritoneal fluid varied from 18,500 to 25,000 over a period of fifteen weeks, including twenty-two observations. Examinations of the smears of the peritoneal fluid of these 5 control animals showed that the proportion of macrophages at the start varied from 88 to 90 per cent. In the remaining examinations, over the next fourteen weeks, the percentage of macrophages in the control animals varied from 83 to 90, although one reading at six hours was 78 per cent. The proportion of eosinophils varied from 5 to 15 per cent and in most tabulations the range was from 5 to 10 per cent. The small lymphocytes varied from 2 to 6 per cent of the total number of cells, and the pseudo-eosinophilic or heterophilic leukocytes never constituted more than 0.5 per cent. These leukocytes were always counted but it is entirely probable that a slight amount of blood was introduced into the peritoneal cavity while the abdominal wall was being punctured and thus increased the percentage of these cells.

In the 4 animals which were on a restricted intake of water for two weeks, the total cell count of the peritoneal fluid varied greatly. When these animals were again given water freely, the cell count dropped and then rose to its original level. The percentage of the different types of cells, however, did not vary with the volume of intake. The percentage of macrophages ranged throughout the period of observation from 81 to 90. The percentage of eosinophils varied from 7 to 12, and that of lymphocytes from 2 to 6 per cent of all cells present.

In the next experiment, 3 animals were given 25 r of radiation and three animals 50 r. All 6 animals were provided water freely and observations were started immediately after irradiation. The cell count of the peritoneal fluid of those animals that received 25 r dropped to less than normal for the first four weeks and then varied from subnormal to a normal level. The average cell count of the group that received 50 r remained around normal, except for a rise during the fourth, fifth, eighth, and ninth weeks after irradiation.

In the animals that received 25 r and in those that received 50 r, two changes were observed in the stained smears, the first being a rapid increase of the percentage of macrophages. This increase, of about 6 per cent, occurred within the first few hours following irradiation and the proportion of macrophages remained at this elevated level. The second change was a gradual increase in the percentage of lymphocytes at the end of the first week. At this time the percentage of lymphocytes had almost doubled and it remained at this level until the end of the period of observation. The increase in macrophages and lymphocytes took place at the expense of the eosinophils.

In the next experiment 11 animals were given the same dose of radiation which had been given to the animals in the experiments on peritonitis, that is, a total of 100 r in two treatments, four hours apart. Six hours after the initial irradiation, the average peritoneal cell count rose 5,000 to 6,000 cells per cubic millimeter. These levels gradually dropped to control values at the end of the second day but then rose again, increasing from the average control levels of 14,000 to 16,500 cells per cubic millimeter to 32,000 to 33,000 cells per cubic millimeter at four weeks. Remaining at this height for two weeks, the average level dropped again to 22,000 cells and until the end of the fourteenth week ranged between this figure and 28,000 cells per cubic millimeter.

In this group of animals, during the control period before irradiation, the macrophages comprised about 80 per cent of the total number of cells, the eosinophils about 8 per cent, and the lymphocytes 8 to 9 per cent. This percentage of distribution remained about the same until the seventh day after irradiation, when the percentage of macrophages started to rise. During the fourth week, it increased to 87 per cent and, with minor variations, gradually increased until it reached 91 per cent at the fourteenth week. The proportion of eosinophils and lymphocytes gradually declined to levels between 4 and 5 per cent.

In another group of 9 animals, which received 100 r at one time, the observations were similar to those on the group in which the 100 r had been given in two treatments, four hours apart. There was a rise of the total cell count at the end of six hours, followed by a transient fall and then a second sustained rise. The differential percentages also corresponded to those in the group that received 100 r in two treatments. There was a slight initial rise of the percentage of macrophages at six hours, followed by a decline, with another rise at the end of two days, followed by a short fall and then a sustained plateau that reached 92 per cent.

In the two groups receiving 100 r, 20 animals in all, two facts were demonstrated: (1) The average total peritoneal cell count increased at two periods after irradiation. The first increase appeared within six hours and may explain the somewhat favorable effect of roentgen rays in the experiments with peritonitis. A second rise of the total cell count took place about one month after irradiation and was sustained for a period of several weeks. (2) Coincident with the rise of the total number of cells there was an increase in the percentage of macrophages. One hundred roentgens is apparently a sufficient amount of irradiation to act as an irritant to the peritoneal membrane.

In the next study 4 animals were given 200 r. The average total peritoneal cell count in these 4 varied from 29,000 to 33,000 cells per cubic millimeter during the control period. Two hours after irradiation, the cell count increased to 36,000; it was less than normal at six hours but had risen again to normal at twelve hours. It then dropped to 20,000 where it remained for two weeks. At the third week the total count was normal and from the sixth to the ninth week it varied up to 40,000, dropping back to slightly less than normal from the ninth week to the end of the experiment. The percentage of macrophages during the control period was 78 to 80; following irradiation, it increased to 91 per cent at the fifth week. This rise was continuous and at no time after the first two days did the per-

centage drop to less than 81. The proportion of eosinophils, which had been 20 per cent during the control period, dropped to 10 per cent after irradiation and maintained this level throughout the experiment. The lymphocytes started at 4 per cent and, after a drop which lasted several weeks, attained a level of 6 per cent.

In summarizing these results two facts again should be noted: (1) The cell count in all the animals in the groups receiving 200 r dropped sharply after irradiation. The abruptness and degree of the drop and the length of time that the count remained less than normal depended directly on the amount of radiation received. (2) There was a rapid increase of the percentage of macrophages following irradiation. The sharpness of this rise, its height, and duration also depended directly on the amount of radiation.

In these and the subsequent experiments, the amount of fluid, as determined by the ease with which it entered the capillary pipet, appeared to increase after irradiation. This increase of fluid may explain the rapid diminution of the cell count. The destructive action of the roentgen rays on the cells appeared in these animals. Hence, it is probable that two mechanisms complemented each other: (1) Irradiation apparently induced an increase of the amount of fluid, with a resultant dilution of the cells. (2) The destructive action on the cells likewise induced a decrease of the total cell count. This destruction may account for the relative increase in the proportion of macrophages, since they are more radioresistant than the other cells normally present.

Five animals were given 400 r. The cell count in the peritoneum of these animals following irradiation dropped even more abruptly, and fell to a lower level than in the group that received 200 r, and gradually tapered off to a subnormal level. The proportion of macrophages started at 78 to 84 per cent and at the end of the first day reached a height of 90 per cent, which it maintained for the next five weeks. At four days the percentage of macrophages reached 95 and continued slightly less than that for the next two weeks but at the end of the fifth week the percentage fell to less than 90 and gradually leveled off to around 85, where it remained.

Five animals were then given 400 r and two days later an additional 300 r, making a total of 700 r. After the second dose, of 300 r, routine observations were continued for twenty weeks. Three control counts varied from 21,000 to 26,000 cells per cubic millimeter. Following irradiation the cell count varied around 18,000 for the first twenty-four hours, dropped to 11,000 on the second day, and then gradually came up to a normal level at the end of two weeks. The cell count remained normal until the seventh week, at which time it fell slightly. It remained between 17,000 and 20,000 until the twentieth week, when it rose to a normal value of 21,800 cells per cubic millimeter.

The proportion of macrophages during the control period varied from 81 to 86 per cent. But three hours after the second irradiation the percentage had increased to 90; at eighteen hours it had reached 95 and for the next two weeks it varied from 93 to 96. After the third week, the percentage varied from 85 to 89; at the seventh week it rose to 91 but thereafter varied between 84 and 87 per cent throughout the remainder of the twenty weeks. The increase of macrophages took place at the expense of the eosinophils, which fell from 15 to 3 per cent, while the proportion of lymphocytes declined from 2 to less than 1 per cent. At the end of one week the lymphocytes returned to a normal level and at the third week the eosinophils started to come back. At the end of the fourth day, the macrophages appeared definitely immature and then gradually approached the mature form. Undoubtedly a dose of this size is sufficient to have a destructive effect on the macrophages as well as on the other more radiosensitive cells. Heterophilic or pseudo-eosinophilic leukocytes appeared in numbers up to 2 per cent after nine hours but disappeared in two days. Apparently a moderate

amount of radiation is required to call these leukocytes forth into the peritoneal fluid of the normal guinea-pig.

Five animals were given 400 r, with 300 r two days later and another 300 r two days after this, making a total of 1,000 r. Observations were started immediately after the completion of the second 300 r and extended for twenty weeks. Three control counts of the total number of cells varied from 16,000 to 19,000 per cubic millimeter of fluid. Nine hours after the last irradiation, the count had dropped to 12,500 and gradually decreased to 10,000 at the end of the second day. By the third week the count had risen gradually to a normal level, where it remained, except for a drop at the eighth, the twelfth, and the fourteenth week. The count reached a normal level of 19,500 at the end of the twentieth week.

The percentage of macrophages varied from 88 to 91 during the control periods, but three hours after irradiation the percentage had increased to 95 and remained between 93 and 97 for the next two weeks. From the third to the seventh week, the proportion of macrophages varied from 91 to 92 per cent and from then on dropped to less than 90, wavering between 84 and 89 per cent for the remainder of the experiment. At the fourth day all macrophages were extremely immature. After irradiation, the percentage of eosinophils and lymphocytes dropped to very low levels. The proportion of lymphocytes fell rapidly from 2.0 to 0.5 per cent, where it remained for the first two days, after which it gradually increased. Heterophilic or pseudo-eosinophilic leukocytes reached levels of 3 per cent during the first nine hours but disappeared at the end of two days.

COMMENT

An analysis of these data warrants several conclusions which are of importance. Doses of roentgen rays less than 100 r have little effect on the cell count of the peritoneal fluid of the guinea-pig but do cause a relative increase of the percentage of macrophages and lymphocytes. A dose of 100 r induced an increase of the total cell count. Doses of 200 r or more caused a decrease of the cell count but a relative increase of the percentage of macrophages. This increase of the macrophages may well explain the resistance of the peritoneal cavity to infection four to six weeks after irradiation.

If the action of roentgen rays on inflammation is due to a destruction of leukocytes and the liberation by them of antibodies, then theoretically a large dose should be of greater benefit than a small one. If, however, the action is due to a proliferative increase of mononuclear cells, particularly the macrophages, then the small doses should be of more value than large ones. The data indicate that 50 r did not cause any increase of the total cell count but did increase the percentage of macrophages, whereas 100 r induced an elevation both of the total number of cells and of the percentage of macrophages. Although these doses are destructive to a mild degree, because of this they are irritants as well. The studies have tended to show that a dose of 50 or 100 r precipitated more of an irritant effect than a destructive one. Doses less than these amounts did not have any apparent or immediate effect on the cell count and doses greater than these had a destructive effect that appeared early. It would seem that roentgen doses of 50 or 100 r, which produce an irritant effect on the peritoneal fluid of the guinea-pig, may be of definite value in the treatment of peritonitis in that animal.

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REFERENCES

1. ALTEMEIER, W. A., AND JONES, H. C.: Experimental Peritonitis: Its Prevention by Roentgen Irradiation. J. A. M. A. **114:** 27–29, Jan. 6, 1940.

2. BELL, E. T.: A Textbook of Pathology. Philadelphia, Lea & Febiger, Ed. 4, 1941.

3. CHROM, S. A.: Studies on the Effect of Roentgen Rays upon the Intestinal Epithelium and upon the Reticulo-Endothelial Cells of the Liver and Spleen. Acta radiol. **16:** 641–659, 1935.

4. CORPER, H. J.: Attempts to Reduce the Resistance of the Guinea-pig to Tuberculosis by Means of Various Agents: Effects of the Roentgen Ray, Benzene, Thorium X, Tuberculin, Ether and Chloroform. Am. Rev. Tuberc. **2:** 587–603, December 1918.

5. CORPER, H. J., AND CHOVEY, P.: Effect of Roentgen Ray and Thorium X on Pneumococcus and Streptococcus Infection in Mice. J. Infect. Dis. **27:** 491–498, 1920.

6. DESJARDINS, A. U.: Dosage and Method of Roentgen Therapy for Inflammatory Conditions. Radiology **32:** 699–705, June 1939.

7. DIXON, C. F., AND RIXFORD, E. L.: Cytologic Response to Peritoneal Irritation in Man: Protective Mechanism. Am. J. Surg. **25:** 504–511, September 1934.

8. HEKTOEN, L.: Influence of the X-ray on the Production of Antibodies. J. Infect. Dis. **17:** 415–422, 1915.

9. HEKTOEN, L.: Further Studies on the Effects of the Roentgen Ray on Antibody-Production. J. Infect. Dis. **22:** 28–33, 1918.

10. HEKTOEN, L., AND CORPER, H. J.: Effect of Injection of Active Deposit of Radium Emanation on Rabbits with Especial Reference to Leukocytes and Antibody Formation. J. Infect. Dis. **31:** 305–312, October 1922.

11. KELLERT, E.: On the Increased Susceptibility of X-rayed Guinea-Pigs to Inoculation with Tubercle Bacilli. J. M. Research **39:** 93–101 September 1918.

12. KELLY, J. F.: Personal communication to the author.

13. KELLY, J. F., AND DOWELL, D. A.: Roentgen Treatment of Acute Peritonitis and Other Infections with Mobile X-ray Apparatus. Radiology **32:** 675–692, June 1939.

14. K'O, Y. K., TU, C. L., AND CHAN, B. C.: Effect of Hard Roentgen-Rays on Intestines of Normal Dogs Fed on Inorganic Iron Compounds. Surg., Gynec. & Obst. **73:** 333–340, September 1941.

15. MAXIMOW, A. A.: A Text Book of Histology. Completed and edited by William Bloom. Philadelphia, W. B. Saunders Co., 1930.

16. MCCLURE, R. D., AND ALTEMEIER, W. A.: Acute Perforated Appendicitis with Peritonitis: Report of 252 Consecutive Cases. Ann. Surg. **105:** 800–814, May 1937.

17. MENKIN, VALY: Studies on Inflammation: Isolation of the Factor Concerned with Increased Capillary Permeability in Injury. J. Exper. Med. **67:** 129–144, January 1938.

18. MENKIN, VALY: Inflammation. Direct Effect of Changes in the Hydrogen Ion Concentration on the Leukocytes. Arch. Path. **27:** 115–121, January 1939.

19. MICHELS, N. A.: Susceptibility of the Omentum of Rabbits to a Single Erythema Dose (400 r) of Roentgen Rays. Am. J. Anat. **52:** 333–395, May 1933.

20. MONTGOMERY, L. G.: Preliminary Study of the Cells of the Peritoneal Fluid in Certain Laboratory Animals. Proc. Staff Meet., Mayo Clin. **7:** 589–591, Oct. 13, 1932.

21. MORTON, J. J.: A Rapid Method for the Diagnosis of Renal Tuberculosis by the Use of the X-rayed Guinea-Pig. J. Exper. Med. **24:** 419–427, October 1916.

22. OSUGI, S.: Über die Strahlenbehandlung der akuten diffusen Peritonitis. Ztschr. d. japan. chirurg. Gesellsch. **36:** 110–111, 1935.

23. OWEN, C. R.: The Bacteriology of Perforation Peritonitis. Thesis, University of Minnesota Graduate School, 1939.

24. PENDERGRASS, E. P., AND HODES, P. J.: Roentgen Irradiation in the Treatment of Inflammations. Am. J. Roentgenol. **45:** 74–106, January 1941.

25. REA, C. E.: Problem of the Treatment of Peritonitis: Preliminary Report. Surg., Gynec. & Obst. **73:** 193–205, August 1941.

26. RICH, A. R.: Inflammation in Resistance to Infection. Arch. Path. **22:** 228–254, August 1936.

27. SEELEY, S. F., HIGGINS, G. M., AND MANN, F. C.: Cytologic Response of the Peritoneal Fluid to Certain Substances. Surgery **2:** 862–876, December 1937.

28. SIMONDS, J. P., AND JONES, H. M.: The Influence of Exposure to X-rays upon the Formation of Antibodies. J. M. Research. **33:** 183–196, November 1915.

29. STEINBERG, B.: Inflammation of Serous Surfaces: Transfer of Living Leukocytes and the Effect on Acute Infectious States. Arch. Path. **25:** 785–791, June 1938.

30. STEINBERG, B., AND DIETZ, A.: Inflammation of Serous Surfaces: Hydrogen Ion Concentration in Relation to Cell Type. Arch. Path. **25:** 777–784, June 1938.

31. STEINBERG, B., AND MARTIN, R. A.: Inflammation of Serous Surfaces: Factors Modifying the Types of Cell Response. Arch. Path. **25:** 792–801, June 1938.

32. TAYLOR, H. D., WITHERBEE, W. D. AND MURPHY, J. B.: Studies on X-ray Effects: Destructive Action on Blood Cells. J. Exper. Med. **29:** 53–73, January 1919.

33. WARTHIN, A. S.: Experimental Study of the Effects of Roentgen Rays upon the Blood-Forming Organs, with Special Reference to the Treatment of Leukemia. Internat. Clin. **4:** 243–277, 1906.

Experimental Studies of the Mechanism of Action of X-Ray Therapy upon Infection[1]

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THE LITERATURE contains much evidence that properly administered x-ray therapy has a beneficial effect upon certain acute and chronic infections in man. (For summary, with bibliography, see Desjardins, 1.) There is also much evidence in support of a contrary opinion. We are not in this paper concerned with this controversy. Whatever the effect in man, the studies to be reported here indicate that in rabbits x-ray irradiation is followed by a large, significant, and consistent reduction in the mortality from toxemia of bacterial origin, and that it produces this effect by causing the liberation of an antitoxic factor. The experimental data from which these opinions were formulated have been reported in detail elsewhere (2). In this discussion they will be briefly summarized.

The study as originally conceived had for its purpose some measure of the effect of both the sulfa drugs and x-ray therapy upon peritoneal infections in rabbits. It was planned to infect the peritoneum by the various experimental methods reported in the literature, but it so happened that the first method used, the intraperitoneal injection of a pathogenic culture, gave rise to certain observations which radically changed the course of the investigation.

From three cultures of hemolytic *Escherichia coli* isolated from different sources there was obtained one which was pathogenic for rabbits. Its minimal lethal dose was established at two slants of a 48-hour culture. Since this microorganism is a rapidly growing one, two 48-hour slants represent a large dose and, although this amount caused profound prostration within two or three hours and led to death usually within nine hours and always within twelve hours, it was impossible to use less. A smaller dose was not consistently lethal, for if the animals survived longer than twelve hours they usually recovered. The lethal result from the intraperitoneal injection of this culture was uninfluenced by the sulfa drugs, regardless of the time or route of administration. That is, these drugs were ineffectual when given either orally or parenterally, or when applied directly to the peritoneal surfaces, prior to, at the same time as, or following the injection of the culture. The cause of failure of the drugs was elucidated by subsequent observations.

An investigation of the effect of x-rays upon these peritoneal infections was suggested by the clinical results reported by Kelly and Dowell (3). The rays were delivered, according to a constant fixed formula, through one anterior port covering the entire abdomen, with the remainder of the body shielded with lead. The factors were: 140 kv. constant potential, 15 ma., an adherent filter of 3.0 mm. aluminum and an added filter of 0.5 mm. copper and 1.0 mm. aluminum at 50 cm. target skin distance. The intensity was 20 r per minute measured in air. The dosage was determined by the duration of exposure, which was the only variable.

POST-INOCULATION IRRADIATION

A first series of 10 animals were irradiated immediately after the intraperitoneal injection of the culture. All died within five hours, as did the controls which were injected simultaneously. Thus irradiation administered after inoculation was of no avail.

[1] From the Departments of Surgery, Radiology, and Physiology, University of Nebraska, College of Medicine, Omaha, Nebraska. Read before the Section on Radiology, American Medical Association, Atlantic City, N. J., June 1942. Accepted for publication in August 1942.

PRE-INOCULATION IRRADIATION

In a second series radiation in doses of 100 to 600 r was given at intervals prior to inoculation, varying from sixteen weeks to twenty-four hours. Half of the animals which received 100 r of radiation twenty-four hours prior to inoculation survived and those that died lived longer than the controls. Of the 6 rabbits which received 100 r forty-eight hours before inoculation, 4 or 66.6 per cent survived. Among the animals irradiated three days before inoculation, 50 per cent survived, and among those receiving 100 r five and seven days before inoculation there was a survival rate of 25 per cent. In the remaining groups, constituted by those which received irradiation more than seven days prior to inoculation, there were no survivors. All animals used as controls throughout these experiments died within twelve hours. Thus it must be concluded that irradiation provided a considerable degree of protection against this otherwise lethal culture. Furthermore, it is apparent that time was required for this protective factor to develop. It was present in twenty-four hours, had attained maximum effectiveness in forty-eight hours, and was then rapidly dissipated.

As stated above, it required a large number of microorganisms to cause death consistently. Thus it would appear that the microorganisms used were of low virulence, as is characteristic of the *Esch. coli* group of bacteria. The necessity of using this large dose plus the onset of prostration within two or three hours suggested the probability that death was due to toxemia and not to peritonitis. It was decided, therefore, to determine the effect of inoculations of the peritoneal cavity with killed cultures. These were found to be essentially as lethal as live cultures. Furthermore, a repetition of the experiments carried out with the live cultures gave essentially the same results when killed cultures were used. Significantly, radiation administered forty-eight hours prior to inoculation gave protection against this toxin to the extent of 60 per cent survivors and a prolonged period of survival for the 40 per cent which died.

From these results there are two logical deductions. First, it is obvious that the culture at the time of inoculation contained a lethal dose of toxin and that any further production of toxin as a result of growth of the bacteria in the peritoneal cavity was superfluous. The cause of failure of the bacteriostatic agents, the sulfa drugs, to influence the course of events is obvious. In establishing a lethal dose with this culture of low virulence it is therefore necessary to use microorganisms in sufficient quantity to supply a lethal dose of toxin. Second, x-radiation exerted some antitoxic action.

There now arose the question of the mechanism of action of x-rays in respect to toxins. It had been observed that, following irradiation over the abdomen, there was an increased quantity of peritoneal fluid which cytologically was essentially normal except for the presence of erythrocytes. When this fluid was recovered in peritoneal washings, mixed with either the live or killed culture, incubated for thirty minutes, and then injected into the peritoneal cavities of stock animals, it gave complete protection. All rabbits so treated survived, while all controls died. Conversely, peritoneal washings from normal untreated animals gave no protection. Thus, it would appear that the peritoneal fluid of the irradiated animals contained the antitoxic factor resulting from the action of x-rays. Since the blood serum of rabbits irradiated forty-eight hours previously manifested this same neutralizing action on toxin, when mixed with either the live or killed culture prior to inoculation, it would appear that the antitoxic factor resulting from irradiation was also present in the blood stream.

EXPERIMENTS WITH DIPHTHERIA TOXIN

Since the studies described above were concerned with a single toxin, an endotoxin, it was decided to carry out another series of experiments to determine whether

the effect was specific or non-specific. For this purpose diphtheria toxin, representative of the exotoxins, was used. Of 16 rabbits which received 100 r of x-radiation over the abdomen forty-eight hours prior to inoculation of a lethal dose of diphtheria toxin, 10, or 62.5 per cent, survived. Of 12 controls, all died. Likewise, the peritoneal fluid and blood serum of the irradiated animals were found to contain the protective factor against the diphtheria toxin, with survival records of 88 and 40 per cent, respectively. All controls in this series died.

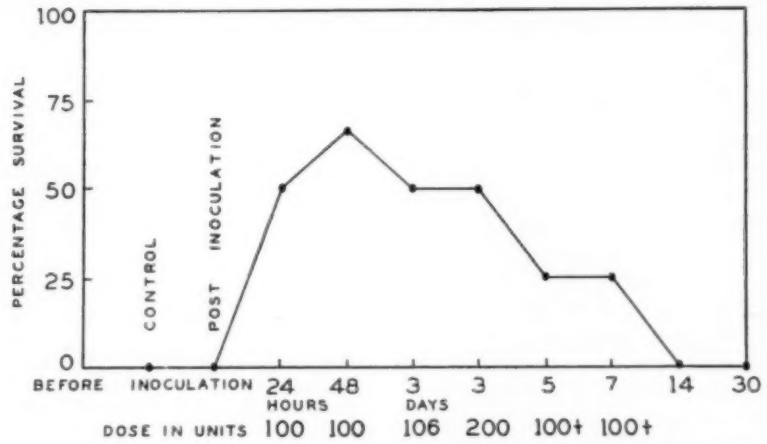

Fig. 1. Percentage of animals surviving inoculation with *Esch. coli* and irradiation. When irradiation was done after inoculation there were no survivors; when it was done twenty-four hours prior to inoculation one-half of the animals survived. Protection reached a peak in forty-eight hours and then was rapidly dissipated. (Courtesy of Ann. Surg., June 1942.)

DISCUSSION

Inadvertently, a series of studies designed to investigate certain aspects of peritonitis became a study of toxemia of bacterial origin and of the effect upon it of x-rays. If in a broad sense a substance which neutralizes or minimizes the effect of toxins can be termed an antitoxic substance, then x-rays were productive of an antitoxic substance in the rabbits used in these experiments. Since this antitoxic factor was present in the blood stream, the protection resulting from irradiation cannot be attributed to local factors inherent in the treated tissues, such as hyperemia, increased or decreased permeability of the capillaries, lymphocytic infiltration, etc., as suggested in the literature.

In an attempt to explain our experimental observations the following theory is offered as a suggestion. X-rays are destructive agents; any stimulating effect on certain types of tissue such as fibrous tissue, as reported, is at the expense of injury to other types of tissue cells. In response to this insult, the cells, or some group of cells, liberate a protective or antitoxic factor. This protective reaction to injury may not be unlike that evoked by various chemical agents, such as snake venom and even bacterial toxins.

Whatever the nature of the protective mechanism, time is required for its development. In our experiments it was present twenty-four hours after irradiation; how much sooner is a problem which will be investigated. It apparently developed too slowly, however, to be of benefit to the rabbits which received irradiation following inoculation. It reached its peak of effectiveness in forty-eight hours and by the seventh day it apparently had been entirely dissipated.

In a recent publication, Harvey, Meleney and Rennie (4) have reviewed the

history of reported investigative efforts to establish peritoneal immunity. They state that chemical irritants, such as aleuronat and starch mixtures, are essentially as effective as vaccines, bacteriogens, and sera in producing non-specific immunity, and that the more irritative the agent the greater the immunity. In this category we believe that x-rays may be included as a physical agent of irritation and destruction.

Conceding that x-radiation gives rise to antitoxic agents, we are faced with the question of the source of these agents. A possible—and even probable—source has been suggested by Pordes (5). He has stated that destruction of leukocytes is the primary and direct effect of irradiation. As a result of disintegration of these cells the antibodies, ferments, and other protective substances which they contain are liberated.

In conclusion, it should be stated that in presenting the results of our experimental study there is no intention of conveying the impression that the mechanism presented was the sole mechanism of beneficial action of x-rays upon infection and toxemia in our animals. There may have been other contributing mechanisms of equal or greater importance.

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BIBLIOGRAPHY

1. DESJARDINS, A. U.: Radiotherapy for Inflammatory Conditions. J. A. M. A. **96:** 401–408, Feb. 7, 1931. Action of Roentgen Rays or Radium on Inflammatory Processes. Radiology **29:** 436–445, October 1937. Action of Roentgen Rays on Inflammatory Conditions. Radiology **38:** 274–280, March 1942.

2. BISGARD, J. D., HUNT, H. B., NEELY, O. A., AND SCOTT, P.: Mechanism of Action of Roentgenotherapy Upon Infection. Ann. Surg. **115:** 996–1006, June 1942.

3. KELLY, J. F., AND DOWELL, D. A.: X-Ray Treatment of Acute Peritonitis. Radiology **38:** 299–306, March 1942.

4. HARVEY, H. D., MELENEY, F. L., AND RENNIE, J. W. R.: Peritonitis: Studies in Peritoneal Protection with Particular Reference to Action of Sulfonamide Drugs in Experimental Peritonitis. Surgery **11:** 244–260, February 1942.

5. PORDES, F.: Über die Natur der Wirkung der Röntgenstrahlen, speziell über das Verschwinden von Anurie nach Nierenbestrahlung. Wien. klin Wchnschr. **36:** 656–657, Sept. 13, 1923. Der Mechanismus der Röntgenwirkung; ein Erklarungsversuch. Fortschr. a. d. geb. d. Röntgenstrahlen **31:** 287–297, 1923–24.

DISCUSSION

James F. Kelly, M.D. (Omaha, Neb.): Almost as soon as x-rays were discovered they were applied therapeutically in both inflammatory and neoplastic diseases. Since dosage factors were poorly understood, it is but natural that the early history of roentgen therapy presents a checkerboard appearance of successes and failures, with the failures predominating. It was not long, however, before some reports were made showing consistently good results in a few diseases.

One of these early reports, by Musser and Edsall (1904), on unresolved pneumonia was followed by others from Heidenhain and Fried on the beneficial effects of the x-ray in postoperative, bronchial, and experimental pneumonia, while further contributions in the lobar pneumonia group were made by Eugene Powell and others, showing in all a mortality between 5 and 10 per cent following roentgen therapy. This approaches, or probably surpasses, the results secured through any other method of treatment of pneumonia without regard to the location or type of the disease. The superiority of roentgen therapy over other agents has been further demonstrated by Rousseau and his co-workers, who have recently reported the recovery of 22 out of 29 pneumonia patients who had failed to respond to sulfonamides.

The record of the x-ray in treating pneumonia has been paralleled by its record, for example, in gas gangrene and acute peritonitis after all other measures, including the sulfonamides, had failed. In all the acute toxic infections, the x-ray is still able to show a high percentage of salvage.

In the experimental field early work by Heinecke, Warthin, Desjardins, Heidenhain, Fried, and others gave evidence of the value of the x-ray in the production of antibodies and the enhancement of the general immunity to acute infection. The work of Jones, Altemeier, Doub, Hartman, and others of the Ford Hospital Group has presented evidence of the value of x-ray therapy in assisting in the production of local immunity in the pelvis in preparation for surgical operation on the rectum and lower colon. From the clinical standpoint, observations of patients with pneumonia, erysipelas, surgical parotitis, gas gangrene, and acute peritonitis furnish impressive evidence of the antitoxic action of small doses of radiation given at short intervals. So striking have been the results in some patients with gas infections, already comatose when the first treatment was given, that there has been no attempt on the part of opponents of radiation therapy to deny the clinical effect. For those, however, who demand experimental evidence Doctor Bisgard's work proves that the toxin introduced into the peritoneal cavity in the rabbit is in some manner

inactivated or neutralized through the action of the x-ray. Fortunately, I believe, for the boys who may soon be wounded in the American Armed Forces, he has included an experiment with the sulfonamides, which showed no beneficial effect.

This latter fact should also bear weight with some clinicians who have been hesitant to use irradiation in acute appendicitis peritonitis, the x-ray treatment of which shows as impressive results as are obtained in gas gangrene. What has been evident clinically for a great number of years to radiologists, should, I believe, now be evident to everyone. The control of toxemia is the essential thing in the treatment of these diseases. The x-ray will control the toxemia better than any other method we have at hand.

For some years past we have insisted that extensive debridement and amputation be deferred in gas gangrene cases until the acute toxic phase has passed and a line of demarcation has formed, since it is the toxemia which kills and not the local disease. I hope that the work of Doctor Bisgard will further reduce extensive debridement and amputation during the acute toxic phase of gas infection and advance our opportunities to apply x-ray therapy for acute spreading peritonitis. Since the x-ray acts upon the toxic feature and the sulfonamides have no such effect, the superiority of the former should be apparent to anyone.

Resolutions were adopted by the American Roentgen Ray Society in 1917, recommending x-ray examination of the chest to eliminate tuberculosis in army recruits. This resolution was not acted upon and its failure to receive consideration has cost this nation over a billion dollars and many lives. As x-ray diagnosis of chest diseases was available in 1917 for the First World War but not utilized to its fullest extent until the present war, so now is x-ray therapy available for the prevention and treatment of wound infection and acute toxic infections in general. It is hoped that we shall not wait until the next war to make use of so simple and safe a therapeutic procedure, which is universally available.

I am sure all radiologists are grateful to Doctor Bisgard for his work and that radiology again must thank someone outside of its specialty for a major contribution to its field.

John S. Lockwood, M.D. (Philadelphia, Penna.): Among surgeons the opinion has been widespread that in evaluating the results of x-ray therapy of acute infections the radiologists have not always taken into sufficient account the tendency toward spontaneous recovery of the lesions which they have treated. In many cases the criteria of success with x-ray therapy have not included mortality statistics —since in most of the localized suppurative lesions for which x-ray therapy has been employed, mortality rates from sepsis are low. Furthermore, even those surgeons who have been willing to concede a measure of benefit from x-ray therapy in suppurative infections have not been convinced beyond reasonable doubt that similar benefit might not have resulted from other therapeutic measures calculated to increase hyperemia in the inflamed area or to supply a specific antibody. In other words, in evaluating x-ray therapy or the use of x-rays in the prevention of peritonitis, one has to consider more than the mere question of whether or not the x-ray is of value. One can concede the value of prophylactic irradiation and still raise a question as to whether that method is preferable to other methods by which a similar end-result can be obtained.

Another factor contributing to the confused status of x-ray therapy in infections has been the multiplicity of theories as to the mechanism of action of roentgen rays on acute inflammation. Consequently work such as that which has been reported by Doctor Bisgard serves to fill a two-fold need: first, it demonstrates through critical experiments that survival of an animal under the conditions employed is determined by whether or not a preliminary dose of x-ray therapy has been administered; second, it presents an important avenue of investigation into the mechanism of the action of x-rays upon normal tissues with particular respect to the influence of such action on resistance to the consequences of infection.

Doctor Bisgard has been so admirably cautious in interpreting his experiments that any further emphasis in this direction may be superfluous. However, certain points seem worth reiteration. The experimental lesion here employed is not an invasive infection in which occurs either actual multiplication of bacteria in the tissue fluids or penetration of host tissues by bacteria. Rather is it a profound toxemia produced by introduction into the peritoneum of bacterial cells which liberate potent toxins after undergoing lysis. It is possible that many other toxic substances, such as hydrochloric acid, injected into the peritoneal cavity would produce a similar effect in the animal. While it is unlikely that many locally injurious agents of non-bacterial origin would be neutralized *in vitro* by peritoneal fluid from irradiated animals as was shown here, it cannot yet be conclusively stated that the protective action of the x-ray treatment has anything specifically to do with the phenomenon of infection and immunity. Before such a conclusion could be reached it would be necessary to demonstrate a protective action in a lesion which could be characterized pathologically as an invasive infection.

From the evidence presented, there can be no doubt as to the fact that the irradiated animal tolerates the intraperitoneal injection of certain toxic substances better than does the non-irradiated animal. It remains to be determined whether this is due to an interference with the intraperitoneal lysis of bacterial cells through which the endotoxins are liberated, to a delay in absorption of toxins by the irradiated peritoneum, or to a non-specific alteration of antigen-antibody relationships. In view of the

survival of some of the controls treated with serum from non-irradiated animals, it does not seem to this discussant that statistical analysis of the evidence yet justifies a conclusion that the blood of irradiated animals contains a toxin-neutralizing factor. There is no doubt, however, that a definitive answer to this question will be reached through continuation of these interesting and promising experimental studies.

As Doctor Bisgard mentioned in the manuscript which he gave me the pleasure of reading, it is possible that the administration of a large amount of plasma protein, in the form of serum, to rabbits subjected to this acute injury would in itself provide a measure of protection. The amounts of serum administered subcutaneously or intravenously were rather large and very likely sufficient to help a great deal in protecting the animal against an acute insult of the type produced experimentally.

It should be emphasized, too, that this work is concerned with prevention of a certain type of lethal reaction to injury and not with treatment of the established reaction. I do not see how this work can be used to the extent that Doctor Kelly suggests in his discussion, to support the routine employment of x-ray therapy in the treatment of established infections. The experimental lesion with which Doctor Bisgard has been dealing is quite a different thing from an established invasive infection. Great injustice would be done to the investigators if their present conservative conclusions were misinterpreted as supporting the indiscriminate use of x-ray therapy in the treatment of peritonitis. The importance of this work lies not in its immediate practical therapeutic application, but in its implication that the rôle of x-ray therapy in infections will yet be placed on a sound theoretical basis.

J. Dewey Bisgard, M.D. (*Closing*): Dr. Lockwood has brought out an important point which I wanted to make, namely, that this is a purely experimental paper and that definite clinical applications cannot be drawn from it. I think it merely helps to answer the question of the mechanism by which x-ray may be effective in infections; that is, acting not directly upon the infection itself—at least in our animals—but obviously merely upon the toxemia.

I also want to make the point that there is nothing in this paper to discredit the effect or the use of the sulfonamides. As I stated in the paper, since these animals received a lethal dose of toxin, any further production of toxin within the peritoneal cavity was superfluous; therefore, if the sulfonamides inhibit bacterial growth, *i.e.*, are bacteriostatic, as we believe, they would have no effect on the outcome.

I think that the 100 per cent survival of the group that received peritoneal fluid from irradiated animals is pretty definite evidence that, whatever the factor is that results from irradiation, it is not dependent upon a local action of the tissues, on absorption, etc., which may play a part, but that there is also some other factor present in the peritoneal fluid.

The group of animals which received the serum plus the toxin is too small for conclusions, but the evidence suggests that this antitoxic factor is present in serum, if it is duplicated in a larger series of animals now under observation.

A Comparative Roentgenologic Study of the Gallbladder by Intensified Cholecystography[1]

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ALTHOUGH MUCH has been written on the subject of cholecystography, there still remain some problems that require further elucidation. A small percentage of normal appearing gallbladders may be pathological, but these are not a serious problem. If a rigid technic is observed, the pathological non-filling gallbladder ordinarily offers little diagnostic difficulty. Some non-filling gallbladders, however, being normal, may give a false impression of pathology. Similarly, a poorly filled or faintly outlined gallbladder presents a difficult problem in diagnosis. Gastro-enterological roentgenologists have become increasingly aware of the possibility and the frequency of false cholecystographic findings, which at times lead to an unwarranted diagnosis and to unnecessary surgical exploration. There are many difficulties in diagnosis that arise to remind us of the inadequacy of the present standardized cholecystographic methods.

In the routine eighteen- to twenty-four-hour roentgenographic study by the single, double, and triple dose methods, the gallbladder, in a small percentage of cases, may present a shadow of poor density, may be only faintly outlined, or for some reason may not fill. For a number of years this was considered to be essentially a matter of dosage and roentgen technic. It now appears that in some instances an increased amount of dye, administered over a longer period of time, is more effective in filling the vesicle, because of the prolonged period of concentration during the stabilization of the gallbladder.

For some reason, certain gallbladders, even though normal, require a longer period of time than others for concentration of sufficient dye-laden bile to produce a satisfactory cholecystogram. The factors responsible for the production of abnormal cholecystograms are not always obvious. An important one, which has been given little consideration, is the effect of gastro-intestinal disorders. Either intrinsic or extrinsic factors, or both, may play a rôle in the filling and non-filling of the gallbladder. Technical factors are likewise highly important. Unsatisfactory results may be due to inadequate preparation of the patient, insufficient dye, faulty technic, overshadowing of the gallbladder by the colon or underlying organs, inadequate absorption of the dye from the intestinal tract, changes in the character of the dye because of change in the *p*H of the intestinal contents, functional changes within the organ itself, as overfilling or the presence of highly concentrated thickened bile, which may prevent the entrance of the dye-laden bile, or some pathologic condition, biliary or extra-biliary. It is well known that a low-fat diet may stabilize the gallbladder to such a degree that it may be kept filled continually, thereby producing a greater concentration of bile, which may be a contributory factor in the production of faint shadows and in non-filling. In order to eliminate this factor, a diet consisting of eggs, milk, cream, and other foods should be ordered from twenty-four to forty-eight hours before the administration of dye.

The intensified gallbladder test is not necessary for the routine study of the gallbladder. The time consumed, the necessity of giving additional dye, the longer period of abstinence from food, the increase in labor and in the number of films make this procedure impractical for routine purposes. In cases of poorly outlined or non-filling gallbladders, however, intensified cholecystography is a real necessity.

[1] Accepted for publication in August 1942.

It is often essential for re-study and elimination of abnormal cholecystograms.

A comparative study of 29 cases has been made to determine the effectiveness of this procedure as a further aid in the diagnosis of gallbladder disease. It is preferable, and at times essential, that the gallbladder be emptied several hours before administration of the dye. The patient is instructed to eat an early breakfast of eggs, cereal, toast and butter, and a glass of milk; a noon luncheon of toast with jelly or marmalade, cup of coffee or tea with lemon; an evening meal of canned fruit salad with lettuce, but no dressing. A single, double, or triple dose of dye may be administered, depending on the type of case, the total dosage ranging from 6 to 25 gm. tetraiodophenolphthalein. If the single dose method is carried out, the dye is administered about two hours after the noon meal. If the double dose method is chosen, one dose is administered in the morning, about two hours after breakfast, and the next dose about two hours after the noon meal. If a third dose is necessary, it is given following the evening fruit salad meal. The patient is instructed to abstain from all medicines and all liquids and foods, with the exception of water and fruit juices and, at the end of eighteen to twenty-four hours, to take an enema and return for the x-ray examination.

Several roentgenograms are made at this time. If these are satisfactory, the examination is completed the same morning. If, on the other hand, the gallbladder is not clearly visible and no obvious intrinsic pathology can be determined to explain the findings, the test should be continued for another twenty-four hours or longer. Immediately following the first examination, two doses of dye are administered, one in the morning, the other in the afternoon. In order to stabilize the gallbladder during the examination, so that a higher concentration of the dye may be produced, it is essential that there be no fat in the special diet during the period of the intensified test. To avoid a prolonged starvation period, the patient is permitted to eat certain foods such as carbohydrates and proteins in the form of vegetables, fruits, and sugars, that are known to have no significant effect upon biliary function. At the end of forty-two to forty-eight hours from the time of the first administration of dye, a second series of roentgenograms is made, including a left oblique view. If at the end of this period the cholecystograms still remain faint, or there is a non-filling gallbladder, one may be more certain of the presence of biliary tract disease.

It is well known that the density of the cholecystogram does not invariably denote a pathologic condition. Variations of density depend upon the concentrating function of the gallbladder, the amount of the dye entering it, and other factors already mentioned. The effect of overshadowing adjacent structures is often given too little consideration. The liver, kidney, psoas muscle, and vertebral column may lessen proportionately the opacity of the cholecystographic shadow. Similarly, a gallbladder which is overshadowed by the colon frequently gives the appearance of lessened density in the cholecystogram. With all of the extrinsic factors taken into consideration, there still remain a certain number of cases in which the gallbladder is poorly visible or does not fill with the dye. If there is any doubt as to the visibility of the gallbladder shadow, then the intensified test becomes an imperative step in the examination. The roentgenologist should never be satisfied with a poor or faintly outlined gallbladder shadow, for such shadows are indeterminate and too uncertain to interpret. A poorly filled gallbladder can mean either a pathologic condition or a normal organ.

In the 29 cases in which the routine eighteen- to twenty-four-hour test and the intensified forty-two- to forty-eight-hour test were made, the following results were obtained. With the eighteen- to twenty-four-hour test, 24 cases showed a faint shadow and 5 a non-filling gallbladder. Following the intensified test, carried out at the forty-two- or forty-eight-hour period, 13 of the cases were considered to

be normal and 16 abnormal. It is of interest to analyze these statistics to obtain detailed information on the effectiveness of the intensified test, as well as to note some of the causative factors which were responsible for the changes noted. In 9 of the 29 cases, the opacity of the gallbladder shadow was slightly improved in the later study, while in 10 cases there was a marked improvement, yielding a normal dense shadow. In the remaining 10 instances there was no difference in the density of the shadow in the two tests. In this group 8 presented faint shadows and 2 non-filling gallbladders. Of 3 gallbladders which produced no shadow following the eighteen- to twenty-four-hour period, 1 became well filled at the end of forty-two hours, while the remaining 2 still did not fill. In these 2 cases failure to fill was due to gallstones.

Among the 29 cases examined, there were 11 instances of gallstones. In 9 of these, the stones were visible, while in 2 cases, diagnosed clinically, the gallbladder failed to fill. In these 11 gallstone cases the cholecystographic test at the eighteen- to twenty-four-hour period revealed a faint shadow in 8 and no shadow in 3. Following the intensified test, the gallbladder shadow remained faint in 3, slightly improved in 2, very good in 3, while in 1 case no shadow was obtained. In the 2 cases that did not fill in the earlier period, a non-filling was still observed after the intensified test. In 2 cases there was a persistent faint gallbladder shadow in both series of examinations, which did not change following a fat meal. These patients were jaundiced. The findings were considered to be due to a pathologic condition of the biliary tract. There were 5 instances of duodenal ulceration in the series of 29 cases. In 2 there was a gastric retention after five hours. All of the 5 cases yielded a faint shadow following the eighteen- to twenty-four-hour examination. In 4 of these the intensified test at the end of forty-two or forty-eight hours produced a good cholecystogram; in the fifth case the gallbladder shadow was improved and was considered normal.

SUMMARY

In a series of 29 cases in which routine cholecystograms showed a faint shadow, a poorly outlined, or a non-filling gallbladder, an intensified cholecystographic study was made. The results offer a factual basis for a more thorough study of those cases which do not present a satisfactory cholecystogram in the usual eighteen- to twenty-four-hour routine roentgen examination. The additional information obtained by the intensified cholecystographic test should leave little doubt as to the necessity for restudying the gallbladder until the roentgenologist is fully satisfied with diagnostic cholecystograms. In most instances any uncertainty due to indeterminate gallbladder shadows can be eliminated if the roentgenologist will give more time to the study of the individual case. The cholecystographic study should be made with sufficient care to assure the greatest possible accuracy in diagnosis. Of the 29 cases in which abnormal roentgen findings were encountered in the eighteen- to twenty-four-hour examination, 13 gave a normal and 16 an abnormal picture following the intensified test.

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Air Myelography for Demonstration of the Cervical Spinal Cord

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THE DEMONSTRATION of the cerebral ventricles and the subarachnoid spinal pathways by the direct introduction of air was first recognized and applied as a diagnostic procedure by Wideroe (20) and Dandy (4). Bingel and Jacobaeus (11) pointed out the value of air injection by means of the lumbar route and succeeded in demonstrating blockage of the spinal pathways in the lumbar and lower thoracic areas. Reichert (17) and Brockbank (1) used air as a contrast medium to demonstrate intraspinal structures, following the use of air myelography in the lumbar area by Coggeshall and von Storch (3) and by Van Wagenen (19). The method was also utilized by Chamberlain and Young (2) in the study of spinal lesions, especially those in the lumbo-caudal sac. Recently the demonstration of intraspinal dermoid tumors has been accomplished by List (14).

Previous investigators have noted the presence of air in the upper cervical region following encephalography and occasionally ventriculography and have utilized this observation in the examination of the spinal cord. Pendergrass, however, has pointed out that, while air has been utilized to outline the intraspinal structures, limited success has been obtained except in the cervical region (15). Here, as in the lumbo-caudal area, the boundaries of the subarachnoid space are sharply delineated by the air so that any change of configuration of the spinal canal appears in the roentgenogram.

The demonstration of a lesion of the spinal cord may present a special problem

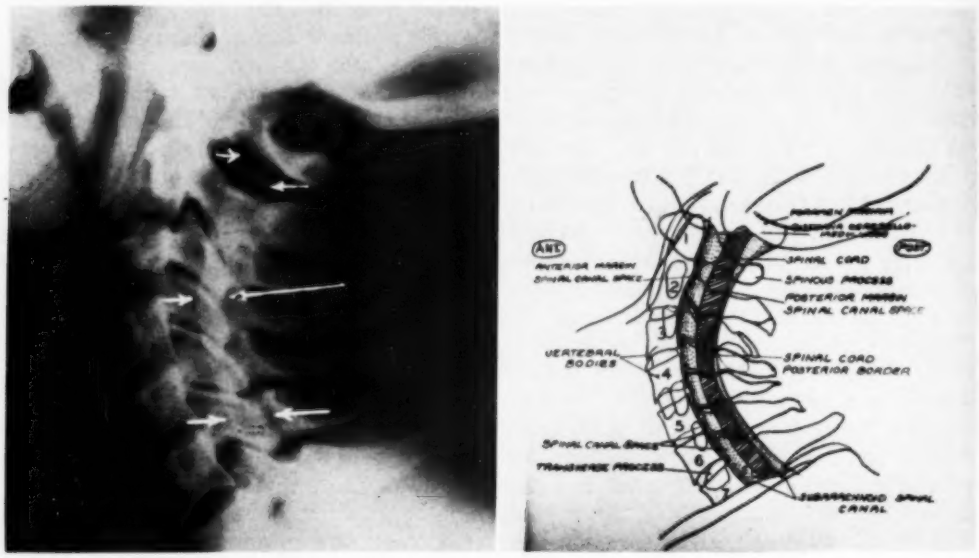

Fig. 1. Normal spinal cord following removal of the spinal fluid and introduction of air. The margins of the cord are designated by the arrows. The examination was made in the Caldwell position with the film alongside the shoulder. In the diagrammatic tracing, the stippled area represents the spinal canal filled with air.

[1] From the Departments of Radiology of the Graduate Hospital of the University of Pennsylvania, Philadelphia, Penna., and Grace Hospital, New Haven, Conn. Accepted for publication in August 1942.

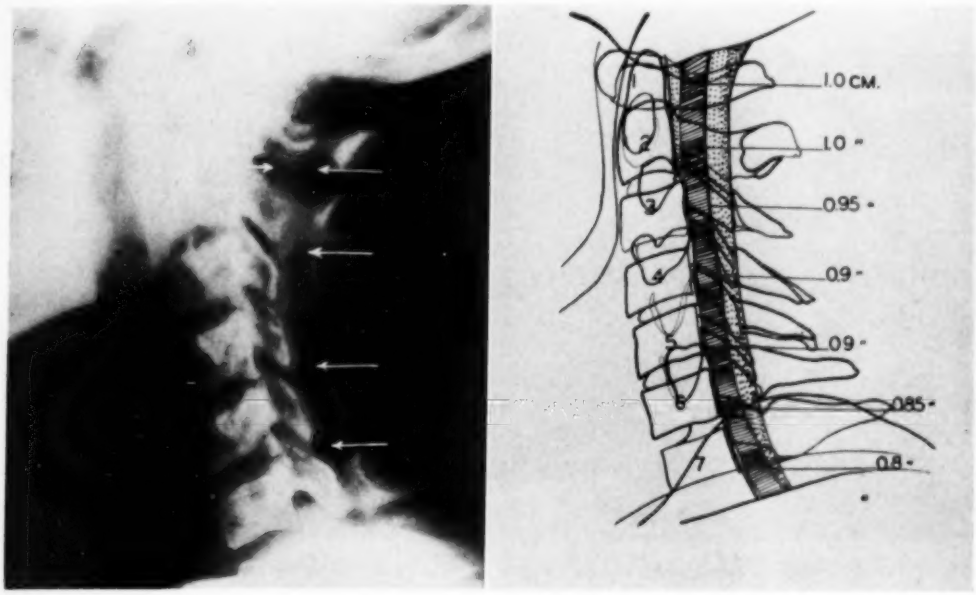

Fig. 2. Normal myelogram of the cervical area. The posterior limits of the cord are indicated by arrows. The accompanying diagrammatic tracing shows the average normal measurements for the respective cervical levels.

when no block or diagnostic defect in the opaque myelographic medium is present. In the cervical area, where the lipiodol examination of the spinal pathways is difficult, this is particularly true. Here the position of the patient, the fragmentation of the lipiodol column, and the disconcerting escape of the opaque material into the cranial subarachnoid pathways make detection of small non-obstructing lesions very difficult. Stookey, Elsberg, Mixter and Barr, Ayer and Spurling have discussed examination of the lesions of the cervical cord following the use of lipiodol. As Hampton points out, some of these writers have not found roentgen examinations of the cervical area after lipiodol injection of much value.

Recently an encephalomyelogram was seen suggesting enlargement of the cervical spinal cord. While Dyke and Davidoff (6), Dyke and Elsberg (10), and Pendergrass (15) have published illustrations of the cord following encephalography, no study of the normal roentgen anatomy could be found in the literature. It seemed necessary, therefore, for the sake of comparison, to determine the normal roentgen measurements of the cervical cord as seen in the lateral view following the injection of air into the lumbar subarachnoid spinal pathways (Fig. 1). For this reason, lateral views of the cervical area were made following routine encephalography and in some cases oblique views of the cervical and upper dorsal vertebrae were also obtained (Fig. 2). In addition, numerous encephalograms were reviewed and measurements of the upper cervical segments were made (Fig. 3). That myelographic studies of the spinal cord are important is shown by demonstration of two spinal cord tumors by this procedure within a relatively short period.

In a review of fifty unselected encephalograms, air could be demonstrated in the cervical portion of the spinal canal in all. The air is retained in the cervical area following lumbar injection in the erect position, being prevented from entering the intracranial cavities by partial obstruction at the level of the atlas. This is thought

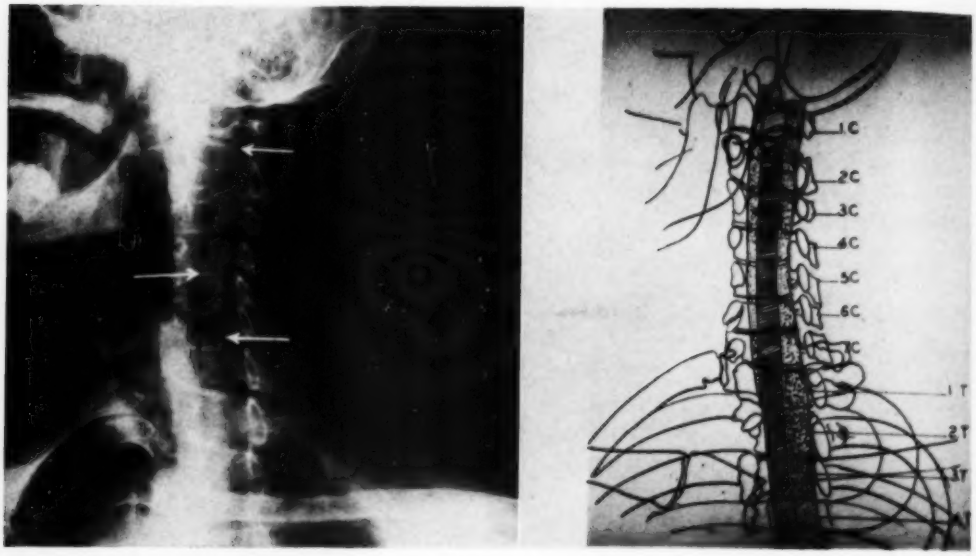

Fig. 3. Oblique view to demonstrate the cord in the thoracic as well as in the cervical area. A diagrammatic tracing is shown on the right.

to be due to the downward projection of the cerebellar tonsils through the foramen magnum, which produces a barrier to the passage of the air.

Dyke and Davidoff (6) believe that air may also be seen in the cervical area following ventriculography. Escaping from the ventricles into the cranial subarachnoid spaces the air may extend into the spinal subarachnoid spaces during the manipulation of the patient. With the patient in the erect posture, the projecting cerebellar tonsils obstruct the air already present in the spinal canal.

While it is beyond the scope of this paper to enter into a description of the anatomy and physiology of the various segments of the cervical spinal cord, a brief discussion of some essential facts may be given. Flattened ventrodorsally, the cervical vertebral canal presents a greater transverse diameter than sagittal. For our purposes, the lower margin of the foramen magnum, or the superior border of the posterior arch of the atlas, constitutes the uppermost limit of the cervical portion of the spinal cord. The meninges, the dura mater, arachnoid, and pia mater are similar to the membranous coverings of the other portions of the central nervous system. The cervical enlargement (*intumescentia cervicalis*), due to the increased number of neurons entering and leaving by way of the cervical and brachial plexuses, represents the greatest expansion of the cord, opposite the level of the fifth and sixth cervical vertebrae. This enlargement is almost entirely in a transverse direction. A study of cross-sections of the cervical cord shows that the transverse diameter may be as great as 14 mm., while the sagittal diameter varies between 6.5 and 9 mm. Measurements of the spinal cord as demonstrated in the lateral cervical air myelogram are given in Table I. These findings are based on a series of 80 encephalograms in which the upper cervical area is included in a lateral film of the skull, and 30 cases in which lateral studies of the cervical area followed pneumomyelography. A larger series of cases is being compiled. Laminographic studies of the cervical spinal cord have also been undertaken.

Normally, according to Dyke and Elsberg, there is a space of about 0.5 cm. be-

TABLE I: MEASUREMENTS OF THE SPINAL CORD IN NORMAL ENCEPHALOGRAMS AND MYELOGRAMS (SAGITTAL VIEWS) FOR COMPARISON WITH CHANGES PRODUCED BY TUMORS OF THE CORD

Vertebral Levels Cervical Measurement	Minimum Measurement (mm.)	Maximum Measurement (mm.)	Average Measurement (mm.)
1	0.8	1.1	1.0
2	0.8	1.1	1.0
3	0.75	1.0	1.0
4	0.75	1.0	0.95
5	0.75	0.9	0.9
6	0.75	0.9	0.9
7	0.75	0.9	0.9

tween the surface of the spinal cord and the wall of the vertebral canal. Although the cord is suspended in the canal by the spinal roots and the dentate ligaments, it retains a certain limited mobility both in the longitudinal and transverse directions (10). Actual movement of the cord in the dural sac is very slight. Small changes in the position of the cord segments in relation to the vertebrae are noted during flexion movements of the vertebral column. The effect of various movements upon the position of the cervical cord are at present under investigation.

Examination of the cervical spine for demonstration of the intraspinal structures following air myelography is made in the lateral view, and the method originally suggested by Caldwell for the study of the cervical vertebra is used. By this method the bodies of the cervical vertebrae from the first to the sixth, and often the seventh, are demonstrated. Often, because the shoulders and the muscular development of the neck will obscure detail in the sixth and seventh cervical segments, modified oblique views of the area may be necessary to demonstrate the cord in this region (Fig. 3).

The examination is made with the patient in the erect position with the lateral aspect of the shoulder pressed against the cassette changer or cassette. Fixation is obtained by means of a cellulose sponge between the head and the face of the cassette changer and an immobilization band, so that the median plane of the face is vertical and parallel to the plane of the film. The fourth cervical vertebra is opposite the center of the cassette and the central ray is projected through this point. The technical factors for the average patient (neck thickness 8 cm.) are: 75 kv.p., 50 ma., anode-film distance 72 inches. A high speed Potter-Bucky diaphragm is used.

The curvature and length of the cervical region vary greatly in different subjects. Usually the cervical spine below the axis presents a slight gentle curve, with the convexity directed anteriorly. Somewhat funnel-shaped in the upper portion, the spinal canal space contracts gradually, reaching its narrowest limit at the level of the third cervical vertebra. Beyond this point to the level of the first thoracic vertebra the lumen remains approximately the same. The posterior limits of the canal are grossly defined by a line drawn from the posterior border of the foramen magnum to the points of junction of the spinous processes with the laminae. The posterior borders of the bodies of the vertebrae define the anterior margin of the canal.

From the accompanying diagrams and films it is seen that the curvature and position of the cord vary. Tilney pointed out that in the cervical area, the spinal canal is more nearly filled with nervous tissue than in the lumbar area. In films made following pneumo-encephalography, the cord may be seen in the anterior or posterior half of the spinal canal. Best demonstrated in the region of the upper three cervical segments, possibly because of the larger air space, in the lateral view the cord appears to arise in the anterior or the mid-portion of the foramen magnum. Often the brain stem can be seen and followed down to the region of the foramen magnum, where it becomes continuous with the cord. The triangular area which is especially well outlined, immediately posterior to the cord, is due to the extension of the cisterna cerebellomedullaris. In our series of cases, the anterior margins of the cord have been delineated more clearly than the posterior margins. As noted before, the muscular shadows in the lower neck area may make recognition of

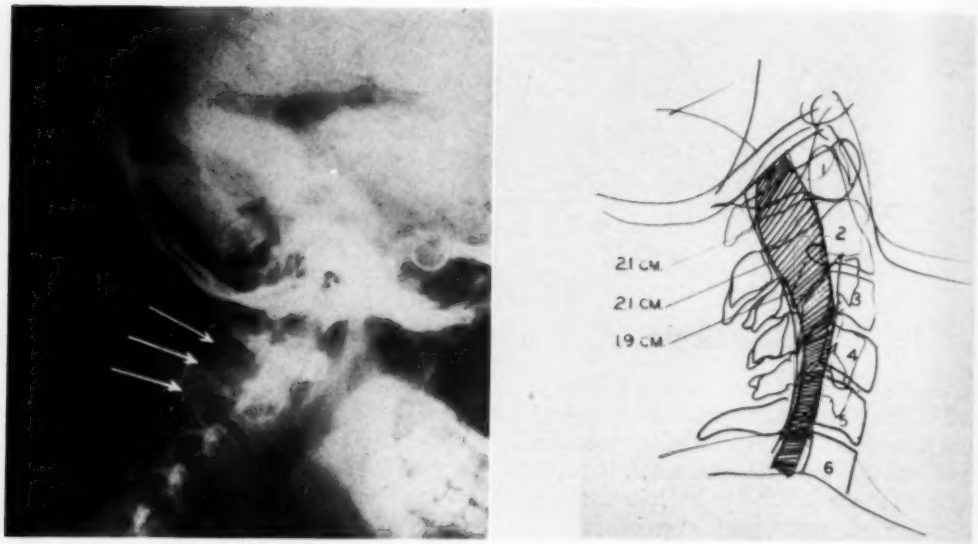

Fig. 4. Case 1: Air myelographic demonstration of an enlargement of the cord in the region of the first, second, and third cervical segments. Operation revealed a mass associated with syringomyelia, with a fluid-filled cavity in this area.

the cord in the region of the sixth and seventh cervical vertebrae difficult. We have not found it necessary to over-expose films in order to obtain adequate contrast and detail. In the average case, the cord in the region of the upper five segments is easily recognized.

Tumors may produce enlargement and deformity of the cord. Syringomyelia, alone and in association with tumors, can also produce a fusiform enlargement. It is our belief that demonstration of the intraspinal structures may make it possible to recognize such lesions in the cervical spinal cord before bone changes distinguishable in the roentgenogram have occurred. Frequently syringomyelia with a cavity filled by a yellow fluid may be associated with a tumor. Kernohan, Woltman and Adson (1931) found a co-existing syringomyelia which extended for a considerable distance up and down the spinal cord in 56 per cent of their cases of intramedullary tumors coming to autopsy (13). Other investigators have shown that both extramedullary tumors and intramedullary tumors may be associated with syringomyelia (10). The distribution of tumors in the cord is shown in Table II, from Rasmussen, Kernohan, and Adson (16).

TABLE II: GENERAL DISTRIBUTION OF 557 CLASSIFIED INTRASPINAL NEOPLASMS

From Rasmussen, Kernohan, and Adson (16)

Cervical area	100 (18%)
Thoracic area	304 (54%)
Lumbar area	117 (21%)
Sacral area	35 (7%)
Multiple levels	1

REPORT OF CASES

CASE 1: T. D. B., a 28-year-old white male, was admitted to the Graduate Hospital Sept. 11, 1941, complaining of pain and burning sensations on the left side of the neck. Since the latter part of July, he had experienced awkwardness, stiffness, and progressive weakness of the left hand, and these changes had become persistent. Paresthesias of the left side of the neck were also noted.

The physical examination revealed weakness dyssynergia, and atrophy of the left interossei muscles, associated with hypertonia. Hyperactive reflexes were present throughout. The left leg showed increased reflexes with weakness. In addition, hypertonia and hyperreflexia were present in the right arm and leg, more especially in the leg. There was tenderness on percussion over the second and third cervical vertebrae.

On Sept. 17, 1941, following encephalography the ventricular system appeared negative. In the upper

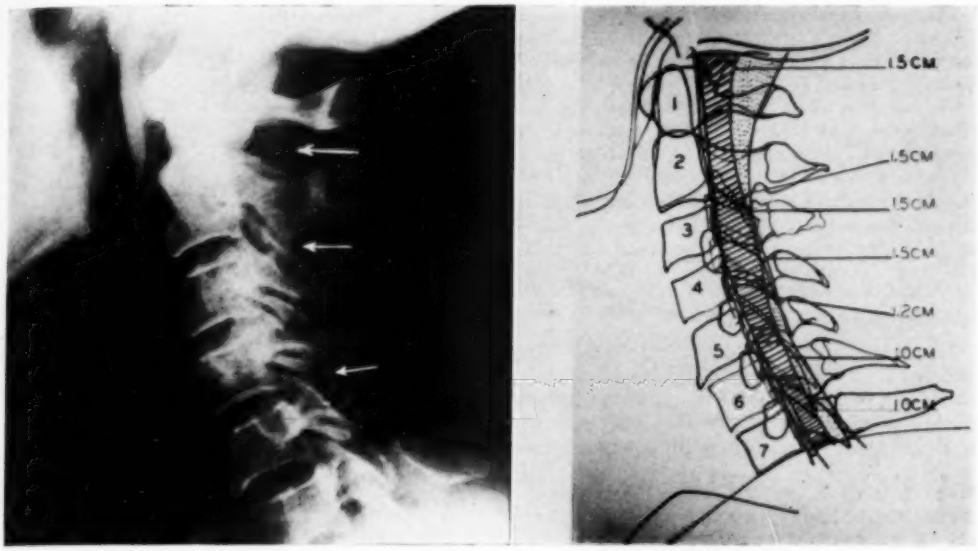

Fig. 5. Case 2: Fusiform enlargement of the cord in the region of the third and fourth cervical segments, as demonstrated by air myelography. Operation revealed an intramedullary mass which microscopically resembled Hodgkin's disease. Compare the measurements in the diagram on the right with the normal values given in Table I.

spinal cord a rounded enlargement was noted (Fig. 4) in the region of the second cervical vertebra. There was also a fusiform enlargement of the cord above and below this region. A tumor of the cord was suspected.

On Oct. 20, Dr. F. C. Grant performed a laminectomy, including the first to the sixth cervical vertebrae. The dura was exposed and appeared broadened. The whole of the upper cervical area of the cord was increased in thickness, and engorged vessels were seen lying over its posterior aspect. On the left anterolateral aspect of the cord, in the region of the second cervical vertebra, a tumor was discovered. The remaining portion of the cord in this region was symmetrically enlarged, both sides appearing to be equally involved. There was, however, greater discoloration of the left side.

After extremely delicate manipulation, the tumor, which lay in the substance of the cord, seemed to collapse. A cystic area must have extended down to the first thoracic vertebra. Inspection at this time showed tumor tissue still infiltrating the lateral aspect of the cord. Microscopic examination showed the growth to be an angioblastoma.

CASE 2: T. F., a 37-year-old Italian male, was admitted to the Graduate Hospital on Oct. 10, 1941, for neurological studies because of weakness of the left arm and shoulder during the past two months. The symptoms had been progressive and now involved the left leg.

In February 1941, the patient had experienced transient pain and weakness of the left hand, followed by interscapular pain. The pains in the left upper extremity were intermittent, but early in March lancinating pains in the left hip were experienced radiating down the thigh to the knee. At the time of admission the patient could rest only when flat on his back.

Examination showed a well defined splenomegaly, weakness of the muscles of the left upper and lower extremities, associated with atrophy and coarse fibrillary twitchings in the deltoid-pectoral-scapular muscle groups on the left side. The tendon reflexes on the left were absent. No pathological reflexes could be elicited. There were hypesthesia and hypalgesia of the left side of the body below the level of the fourth cervical segment.

Repeated examinations demonstrated an enlarged spleen. No enlarged lymph nodes were noted, however, and except for a slight leukopenia there were no abnormal blood findings. The neurological changes were best demonstrated in the lumbar dermatomes (L 1, 2, 3). Clinically, a mid-cervical lesion on the left side, involving the lower motor neurons, was considered as being most likely. Syringomyelia, neoplasm, and progressive muscular atrophy were considered. Because of the clinical findings syringomyelia was considered most probable.

The blood morphology and serology were normal. Spinal fluid pressure was 160 mm. water. The response to jugular compression was normal and no block was demonstrated. The total spinal fluid protein was 111 mg. per cent.

Roentgen examination demonstrated a fusiform dilatation of the cord in the region of the third and fourth cervical vertebrae, believed to be due to a lesion in this area (Fig. 5).

On Nov. 13, 1941, a laminectomy was done, including the first to the sixth cervical vertebrae, revealing an extracordal mass of cartilaginous appearance attached to the right side of the cord in the region of the lamina of the second cervical vertebra. No erosion of the canal by the mass was observed. The posterior roots were cut on the left side from the fifth to the second cervical vertebra. Pathological examination revealed tumor tissue resembling Hodgkin's disease.

NOTE: We are indebted to Dr. Francis Grant and Dr. J. C. Yaskin of the Departments of Neurology and Neurosurgery of the Graduate Hospital of the University of Pennsylvania for the permission to report these cases. In addition, we wish to express our thanks to Mr. Harold E. B. Shea, R. T., Head Technician of the Grace Hospital, New Haven, Conn., for his assistance in the preparation of the illustrations.

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BIBLIOGRAPHY

1. BROCKBANK, T. W.: Mechanical Methods Aiding Localization of Spinal Cord Compression. Virginia M. Monthly **55:** 806–811, February 1929.

2. CHAMBERLAIN, W. E., AND YOUNG, B. R.: Air Myelography in the Diagnosis of Intraspinal Lesions Producing Low Back and Sciatic Pain. Radiology **33:** 695–700, December 1939.

3. COGGESHALL, H. C., AND VON STORCH, T. J. C.: Diagnostic Value of Myelographic Studies of the Caudal Dural Sac. Arch. Neurol. & Psychiat. **31:** 611–613, March 1934.

4. DANDY, W. E.: Ventriculography Following Injection of Air into Cerebral Ventricle. Ann. Surg. **68:** 5, July 1918.

5. DANDY, W. E.: Diagnosis and Localization of Spinal Cord Tumors. Ann. Surg. **81:** 223–254, January 1925.

6. DYKE, C. G., AND DAVIDOFF, L. M.: Pneumo-Encephalographic Appearance of Hemangioblastoma of the Cerebellum. Am. J. Roentgenol. **44:** 1–8, July 1940.

7. DAVIDOFF, L. M., AND DYKE, C. G.: The Normal Encephalogram, Lea & Febiger, Philadelphia, 1937.

8. ELSBERG, C. A.: Concerning the Clinical Features and Diagnosis of Extramedullary Meningeal and Perineurial Fibroblastomas of the Spinal Cord. Bull. Neurol Inst., New York **3:** 124–137, June 1933.

9. ELSBERG, C. A., AND DYKE, C. G.: Diagnosis and Localization of Tumors of the Spinal Cord by Means of Measurements Made on X-ray Films of the Vertebrae, and the Correlation of Clinical and X-ray Findings. Bull. Neurol. Inst., New York **3:** 359–394, March 1934.

10. ELSBERG, C. A.: Surgical Diseases of the Spinal Cord, Membranes, and Nerve Roots. New York, Paul B. Hoeber, Inc., 1941.

11. JACOBAEUS, H.: On Insufflation of Air into the Spinal Canal for Diagnostic Purposes in Cases of Tumors in the Spinal Canal. Acta med. Scandinav. **55:** 555, 1921.

12. KERNOHAN, J. W., WOLTMAN, H. W., AND ADSON, A. W.: Gliomas Arising from the Region of the Cauda Equina. Clinical, Surgical, and Histologic Considerations. Arch. Neurol. & Psychiat. **29:** 287–307, February 1933.

13. KERNOHAN, J. W., WOLTMAN, H. W., AND ADSON, A. W.: Intramedullary Tumors of the Spinal Cord: Review of 51 Cases, with Attempt at Histologic Classification. Arch. Neurol. & Psychiat. **25:** 679–701, April 1931.

14. LIST, C. F.: Intraspinal Epidermoids, Dermoids, and Dermal Sinuses. Surg., Gynec. & Obst. **73:** 525–538, October 1941.

15. PANCOAST, H. K., PENDERGRASS, E. P., AND SCHAEFFER, J. P.: The Head and Neck in Roentgen Diagnosis. Springfield, Ill., Chas. C. Thomas, 1940.

16. RASMUSSEN, T. B., KERNOHAN, J. W., AND ADSON, A. W.: Pathologic Classification, with Surgical Consideration of Intraspinal Tumors. Ann. Surg. **111:** 513–530, April 1940.

17. REICHERT, F. L.: Injection of Air for Localization of Lesions in the Spinal Canal—Pneumomyelography. West. J. Surg. **47:** 297–300, June 1939.

18. SCOTT, MICHAEL, AND YOUNG, B. R.: Air Myelography in the Diagnosis of Lesions of the Spinal Canal. Arch. Neurol. & Psychiat. **38:** 1126, November 1937. See also Am. J. Roentgenol. **39:** 187–192, February 1938; Confinia Neurologica, Separatum Vol. II, Fasc. 7, p. 219.

19. VAN WAGENEN, W. P.: Roentgenological Localization of Spinal Subarachnoid Block by Use of Air in the Subarachnoid Space. Ann. Surg. **99:** 939–943, June 1934.

20. WIDEROE, S.: On Intraspinal Injections of Air and Their Diagnostic Value in Diseases of the Cord, Especially Tumors. Norsk. mag. f. lægevidensk. **32:** 491–495, **1921.**

Roentgen Diagnosis of Lacerated Spleen[1]

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IN CIVILIAN life traumatic injury of an intra-abdominal organ is by no means a rarity, particularly since the advent of the automobile and the mechanization of industry. In perforations of a hollow viscus the radiologist has been of distinct aid to the clinician and surgeon in demonstrating free air beneath the diaphragm. In lacerations of the liver and spleen he has been less helpful. At the present time, under the conditions of global war, careful evaluation of roentgen films, with the object of diagnosing hepatic or splenic injuries, is of special importance. Blast injuries due to bombs may cause rupture of solid or hollow viscera without external evidence. The differentiation of intraperitoneal from extraperitoneal injury may not only be baffling to the diagnostician, but is often of great concern to the surgeon in his concrete approach to a specific case. We shall attempt in this paper to record and analyze the x-ray evidence of splenic lacerations.

ANATOMY OF SPLEEN

The spleen is a soft, highly elastic, contractile organ of purplish color, situated in the upper left posterior part of the abdominal cavity, partly in the epigastrium, mainly in the left hypochondrium. It is molded by the diaphragm, kidney, stomach, and colon. Its dimensions vary widely, but average 12 × 7 × 4 cm. (weight 200 gm.).

The shape of the spleen is modified by the relaxation, distortion, or contraction of the neighboring organs. It is also subject to substantial alteration with physiologic variations. When the stomach is distended and the colon contracted, the spleen has the shape of a segment of an orange; when the stomach is contracted and the colon distended, it has the form of an irregular tetrahedron. In the recumbent position the long axis of the spleen corresponds in direction with the posterior part of the tenth rib. The gastric surface of the spleen is deeply concave, molded by the stomach. It is interrupted by an irregular slit, the hilum, through which the splenic vessels course.

The spleen is entirely covered by peritoneum and is anchored by two peritoneal folds—the lienorenal and gastrolienal ligaments.

DIAGNOSIS OF LACERATION

The symptoms of a lacerated spleen are those of intra-abdominal hemorrhage. Pain may radiate to the left scapula; there may be a tender indefinite mass, rigidity of the overlying muscles, shifting dullness, and shock. Hemorrhage may be violent, resulting in early death; it may be progressive, allowing the patient to walk perhaps a half a mile, with exsanguination following within forty-eight hours, or it may be of the delayed type, characterized by repeated bleeding, usually with violent pain on exertion, at intervals of several days.

Delayed splenic hemorrhage presents a serious catastrophe, which must be recognized promptly if the patient is to survive. A blow or crushing type of injury over the left lower thorax, especially when accompanied by fracture of the lower left ribs, may cause rupture of the splenic capsule hours or days after the initial injury.

The following observations may be helpful in the proper diagnosis of delayed splenic hemorrhage. (1) There is considerable variation in symptoms, depending upon the severity of the injury to the spleen. (2) Rapid exsanguination or vague abdominal signs may be present over a period of days or weeks. (3) A history of

[1] From the X-ray Department, Jewish Hospital, Philadelphia, Penna. Accepted for publication in August 1942.

Fig. 1 Case 1: Left-sided pneumothorax associated with fractured ribs.

direct violence is usually obtainable. (4) Pain in the left upper quadrant or splenic enlargement is the initial symptom.

Delayed hemorrhage from the spleen may result from (*a*) minimal capsular rupture, (*b*) intrasplenic hematoma, or (*c*) perisplenic hematoma.

X-Ray Findings: In a survey of 100 flat plates of the abdomen in persons without splenomegaly, it has been observed that the spleen can very often be delineated fairly well in the left upper quadrant; where the stomach is distended with air the splenic shadow may be discerned with great clarity, but the greater curvature of the stomach retains its normal convexity.

In lacerations of the spleen, there is obliteration of the splenic shadow. This may be due either to an intracapsular splenic hematoma or perisplenic hematoma. In addition to hemoperitoneum, the blood gravitates along the gastrosplenic ligament and infiltrates in juxtaposition to the gastric wall. This results in a jagged, serrated greater curvature. The extent of serration and deformity of the gastric contour is directly proportional to the degree of hemorrhage. Where the latter is pronounced, there is an associated reflex gastric dilatation. The finding of a dilated stomach along with serration of the greater curvature, as mentioned above, is doubly significant and lends further proof to a specific diagnosis of a lacerated spleen.

Occasionally the perisplenic bleeding results in tenting of the diaphragm, which is an additional valuable sign when present (1).

Fig. 2. Case 2: Dilated stomach with marked serration of greater curvature at the cardia and pars media. The splenic shadow is enlarged and ill defined, hugging the greater curvature of the stomach as a result of perigastric hemorrhage.

CASE REPORTS

CASE 1: A. D., 9 years of age, was brought to the accident ward after being struck in the abdomen by a truck. He was experiencing excruciating abdominal pain and was in obvious shock—pallid, cold, and clammy, with feeble pulse, and slightly cyanotic. He cried out at the slightest touch. Occasional peristalsis was audible. There was marked involuntary rigidity with exquisite tenderness throughout.

X-ray examination revealed 60 per cent compression of the left lung by air in the pleural cavity, pushing the heart and mediastinum almost completely into the right side of the chest (Fig. 1). There was an associated hemothorax and subcutaneous emphysema. Because of the abdominal rigidity and fractured left lower ribs, a lacerated spleen was suspected.

Under local anesthesia the abdomen was opened

through a left rectus incision. The spleen was found to be torn about one inch at its lower pole. The laceration was sutured, with implantation of a piece of fat. The other abdominal viscera were normal. The child died on the third postoperative day.

CASE 2: H. F., age 18, struck a tree while sledding, severely injuring his abdomen, which had been extremely tender since the occurrence of the accident, six hours before admission. Pain in the left upper quadrant had become progressively worse. The

Fig. 3. Case 2: Operative specimen, showing extensive laceration of the spleen, through the hilum. There were both an intrasplenic and extrasplenic hematoma.

patient was pale and sweating and was obviously in extreme pain, talking only in a whisper. The blood pressure was 125/75, later dropping to 110/70. The abdomen was exquisitely tender, with protective muscle spasm in the left upper quadrant. Pain was deep seated and referred to the left shoulder. There was no audible peristalsis. The impression was that of a possible ruptured viscus. The white cell count was 18,800, with 95 per cent polymorphonuclears and 6 per cent lymphocytes.

X-ray studies showed the stomach considerably dilated with gas. The duodenal cap was dilated. A small amount of air was seen in the small bowel

Fig. 4. Case 3: Roentgenogram showing fine serration along the greater curvature. The splenic shadow is continuous with the perigastric hematoma.

beneath the stomach. The left margin of the body of the stomach had a serrated appearance (Fig. 2). The spleen seemed to be enlarged and displaced downward. Between the stomach and the transverse colon was a shadow of homogeneous density. Because of the serration of the greater curvature of the stomach and the distortion and displacement of the splenic shadow, a diagnosis of lacerated spleen was indicated.

With the patient under spinal anesthesia, the peritoneum was opened through a left rectus incision. A large amount of blood was disclosed. This was removed by continuous suction, to be employed for auto-transfusion. Exploration revealed a rupture of the spleen through almost its entire width. The spleen was immobilized by traction toward the midline. The splenic vessels were clamped and the spleen removed after cutting between the clamped pedicles (Fig. 3). The patient made a satisfactory recovery.

CASE 3: E. H., a 10-year-old girl, was brought into the accident ward, with dyspnea. In a game of leap frog, her brother had jumped over her back, doubling her over. She immediately complained of pain over her abdomen and difficulty in breathing. Soon thereafter she experienced nausea, but did not vomit. A significant complaint was pain in the left shoulder. The respiratory rate was 20, and respirations were of the grunting type. Breathing was mainly costal. There was an area of ecchymosis in the upper lumbar region posteriorly. Palpation revealed considerable rigidity, most marked in the left upper quadrant. There was some tenderness to percussion over the left ribs.

On x-ray examination the diaphragm appeared soft and spongy. No air was seen subdiaphragmatically. The heart was centrally located, normal in size, shape, and position. The mediastinum was clear. Both lungs were essentially negative. The stomach was greatly dilated, and the small intestine also showed some dilatation. The liver was not enlarged. The spleen was displaced somewhat by the dilated stomach. In the region of the spleen, in the eleventh interspace, was an irregular, jagged line of lessened density, about 2 inches in length. It was believed that this might correspond with a laceration of the posterior aspect of the spleen (Fig. 4).

Operation was done, confirming the presence of a lacerated spleen. The patient made an uneventful recovery.

CONCLUSION

Criteria for the x-ray diagnosis of lacerated spleen are presented. These should be helpful in the evaluation of traumatic injuries to the left upper abdomen and should be of aid to the surgeon in deciding on the proper approach to doubtful intra-abdominal injuries.

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REFERENCE

1. DEAVER, J. M.: Delayed Hemorrhage Following Traumatic Rupture of Spleen with Particular Reference to Roentgenologic Findings: Case Report. Ann. Surg. **113:** 477–480, March 1941.

Roentgen Treatment of Inoperable Ulcerating Carcinoma of the Breast[1]

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IN 1939 DESJARDINS, McCullough, and one of us (Leddy) reported some results of the roentgen treatment of patients suffering from primary inoperable carcinoma of the breast. One of the most distressing features encountered in the group of cases on which that series was based was the high incidence of ulceration and its associated inconvenience and embarrassment to the patient. In the 1939 report there were 67 instances of ulceration among the 212 cases reported. In nineteen of them the ulcers had healed for a time after suitable roentgen therapy. The palliative results reported in the earlier paper prompted us to approach the problem of ulcerated carcinoma of the breast from a slightly different point of view.

From 1925 to 1940, inclusive, 98 patients suffering from primary inoperable ulcerating carcinoma of the breast were treated in the Section on Therapeutic Radiology at the Mayo Clinic. Included in this group were both patients who had had no previous treatment at all and those whose treatment had not conformed to the usually accepted methods. All these patients with ulcerations had been refused operation because they had one or more of the other generally accepted contraindications to surgical intervention; they were patients for whom not even palliative simple mastectomy seemed advisable.

The very first signs or symptoms complained of by these patients were investigated by us with the hope that they might give some clue to causes of delay in seeking proper medical attention during the period in which the disease had reached an advanced stage. It is interesting to note that the chief and only sign complained of by 87 patients was a lump in the breast. Only 4 patients noted both a lump and pain. Two patients stated that their first symptom was retraction of the nipple and the skin surrounding it. Four others noted discharge, crusting of the nipple and a lump, pain, and bleeding from the nipple with pain, respectively. One patient came to the clinic merely for an examination. During routine examination a small ulcerating carcinoma, involving the nipple and quite unknown to this patient, was discovered by the examining physician. The almost total absence of pain in the early stages of carcinoma of the breast was one of the chief reasons for the failure of the patient to consult a competent physician. The mere presence of a lump was interpreted as being nothing serious.

Forty of the patients had sought no medical opinion whatever before their admission to the clinic. The remaining 58 had presented themselves to their local physicians for advice and treatment only after a delay averaging more than fifteen (15.5) months after they knew that some sort of disturbance was present in their breasts. The wide variety of medical attention they had received is worthy of brief attention. Twenty-five of the patients were given sound advice by their family physicians. The other 33 patients were given treatment and/or advice which can hardly be considered sound; that is,

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if it be admitted that there are only two proper methods of treatment—operation and radiotherapy. The measures employed in these cases included the application of pastes and salves, massage or manipulation, the application of heat, electric treatment with lights or sparks or plates, medical management (including diets), incision, and the use of various kinds of apparatus, alone or in combination. The advice given to some of these patients was equally unsound. One physician told his patient the lump was "harmless"; another told her to "forget about it"; and several others had advised women that the lesion was "inflammatory," "cystic," or "muscle and harmless." The patient was thereby deluded into a false sense of security, being led to think that she did not have cancer, but only some of its symptoms.

We were also interested in determining, if possible, what had happened to the 17 patients who had consulted a physician as soon as the first sign or symptom appeared. If a cure is to be expected in cancer of the breast, the optimal time at which to institute the proper procedures is as early as possible. Five of these 17 patients had been advised to undergo operation immediately. They either refused to accept this advice or else delayed until, on their arrival at the clinic about one and a half years later, the lesions in the breast were inoperable and ulcerating. The remaining 12 patients were ill advised or ill treated. Because of a false sense of security, they had delayed their visit to the clinic on an average of about forty months.

It is obvious that the 98 patients of this series represent a group for which the therapeutic outlook is rather discouraging. The best that could be hoped for from treatment was some degree of palliation. The average elapsed time from the onset of the disease to the arrival of the patient at the clinic was twenty-six months. The average age of the patients was fifty-five years. The youngest was twenty-five years of age and the oldest seventy-seven years. The majority were in the sixth decade (Table I).

TABLE I. DISTRIBUTION, ACCORDING TO AGE, OF 98 PATIENTS SUFFERING FROM ADVANCED MALIGNANT TUMORS OF THE BREAST

20–30 years	1
30–40 years	8
40–50 years	22
50–60 years	30
60–70 years	25
70–80 years	12
TOTAL	98

In only 5 instances was there involvement of both breasts. The right breast was the site of carcinoma in 46 patients and the left breast in 47. In 42 cases the area of involvement of the breast was central. Among 35 patients the lesion was situated in the upper and outer quadrant. The remaining sites were equally scattered throughout the quadrants of the breast. In some cases the lesion was so extensive that its point of origin could not be determined.

Only 2 patients were free from metastasis, as determined by clinical or roentgenologic examination. In 37 of the cases axillary involvement was demonstrated. Twenty-six patients had metastatic processes in the lymph nodes in the supraclavicular area. The remaining 33 had visceral or skeletal metastases.

The plan of treatment and the technical factors used in the majority of cases were similar to those reported by Desjardins, McCullough and one of us (Leddy). The method of "converging beams" has continued to prove its value and effectiveness. We now use, in the majority of instances, 130 kv. (constant potential), 6 ma., 40 cm. target-skin distance, and 6 mm. of aluminum filtration, for we know of no method superior to this scheme of treatment. The areas in which treatment is employed are illustrated in Figure 1.

The anterior portion of the thorax on the involved side is divided into four or six sectors, depending on the size of the lesion in the breast, and each sector is centered over the tumor. The central rays are directed toward the center of the sector. These fields are supplemented by axillary and supraclavicular fields on the affected side and, on some occasions, over the

breast, axilla, and supraclavicular space on the unaffected side, particularly when the lesion is situated near the sternum. Other metastatic lesions are treated whenever occasion demands. A dose of 500 to 600 r, measured in air, is given to each sector, at one sitting. Usually, treatment is given to one area (or perhaps two) daily, though some patients are able to tolerate only a half treatment a day; hence the full course may require from four to eleven

cember 1940) revealed the fact that 43 patients were dead. In 24 cases no good follow-up report was available, but these patients likewise had probably succumbed to their disease. Twenty-four patients were still living and stated that they were definitely improved, whereas 7 were worse after roentgen therapy, which in each instance had been incomplete because of the precarious condition of the patient when treatment was started.

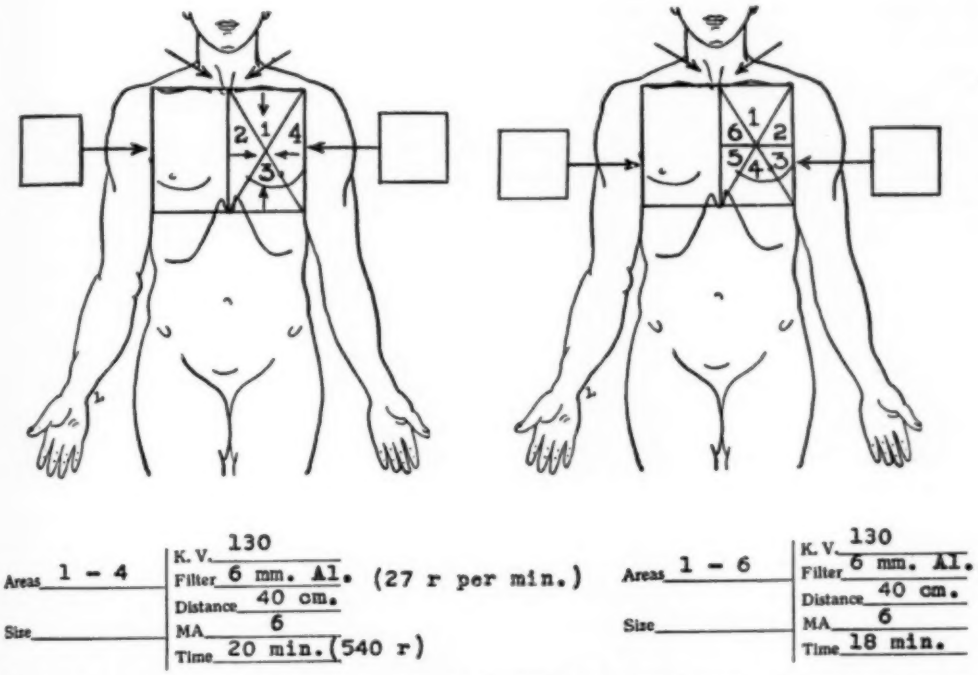


Fig. 1. Anatomic areas and doses employed in the "multiple converging beams" technic of irradiation for ulcerating carcinoma of the breast.

treatment days, depending on the number of fields treated and the extent to which treatment is divided. This series is repeated in a month and again after another month. Subsequent roentgen-ray therapy is administered as the situation indicates.

One patient tolerated ten such courses during a period of four years without the slightest injury to lungs or ribs, and only mild cutaneous changes.

A review of the records of the 98 patients at the conclusion of this study (De-

A survey of the results obtained by the administration of increasing numbers of courses of "multiple converging beam" roentgen therapy is presented in Table II.

The group of patients who received three or more courses of "multiple converging beam" therapy comprised the greatest number with healed or partially healed ulcers. Those receiving one course of treatment showed the poorest results. It should be noted that in this group were many patients who at the time of their ini-

TABLE II: RESULTS OF TREATMENT: "MULTIPLE CONVERGING BEAM" ROENTGEN-RAY TECHNIC AND OTHER FORMS OF THERAPY

Result	Courses of Treatment			Other Treatment§
	1*	2†	3 or more‡	
Ulcer healed	1	6	13	3
Ulcer partly healed	7	1	10	5
Average duration of life after treatment, months	6.9	4.6	18.9	10.5

* 36 cases. † 11 cases. ‡ 28 cases. § 23 cases.

tial treatment were in the terminal stages of the disease, so that failure to obtain a better result is easily explainable.

The average duration of life after the onset of roentgen therapy also presents some interesting considerations (Table II). After one course of treatment, the average duration of life, dated from the time of the first treatment, was slightly less than seven months. Those patients who received three or more courses of "multiple converging beam" therapy lived for slightly more than a year and a half after treatment had been started. We believe that only the patients who were treated three times received adequate roentgen therapy. It must also be remembered that patients in good physical condition who have slowly growing cancers of a relatively low degree of malignancy will survive longer, and hence will be able to avail themselves of as many as three series of treatments. This factor alone is no doubt responsible to some extent for the figures given here.

After treating such a group of patients in the late stages of cancer, we can, as stated previously, hope for little more than temporary palliative results. Two patients, nevertheless, each sixty-five years of age, had had lumps in their breasts for sixty months and seventy-two months prior to their admission to the clinic. Each had a large ulcerating lesion in the upper and outer quadrant of the left breast. The conditions were considered to be inoperable because of fixation and metastasis to lymph nodes. In neither case was biopsy done. These patients received eight and nine courses, respectively, of "multiple converging beam" therapy for a period of four years. Re-examination at the clinic just prior to death from cardiac disease failed to reveal any clinical evidence of a malignant process in either one. We mention these two patients merely to illustrate what can be accomplished in therapeusis. Such results can, of course, never be predicted before roentgen-ray treatment is started, and they are rarely obtained, but it is the occasional unannounced excellent response that keeps the fire of hope burning in a field that has many disappointments.

In evaluating our work we must admit that these results are far from ideal, yet they are noteworthy considering the type of lesion against which they were obtained. In 23 instances the ulcer completely healed and in an equal number of cases its size was reduced considerably. Twenty-four patients claimed that their general condition had definitely improved. As we have mentioned, only 7 patients stated that they were worse after roentgen therapy.

SUMMARY

The foregoing study emphasizes several points: (1) that the hopeless stage of ulceration in which some malignant lesions of the breast are first seen is the result of neglect of the early signs and symptoms; (2) that worth-while palliation can be obtained by judicious roentgen therapy; (3) that in our experience the best palliative results are produced by the method of "multiple converging beam" therapy; (4) that the medical profession in general is still in need of education concerning the diagnosis of cancer, and especially in the matter of adequate treatment of the disease.

Mayo Clinic
Rochester, Minn.

REFERENCE

MCCULLOUGH, J. A. L., LEDDY, E. T., AND DESJARDINS, A. U.: Roentgen Treatment of Primary Inoperable Carcinoma of the Breast. Am. J. Roentgenol. 42: 534–538, October 1939.

Medical Staff Conference on Parathyroid Gland Disease

UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL HOSPITAL, SAN FRANCISCO

Francis S. Smyth, M.D., Mayo H. Soley, M.D., Hans Lisser, M.D., Leon Goldman, M.D., E. R. Miller, M.D., Stuart Lindsay, M.D.

Presentation of Patient (March 18, 1942): Mrs. D. (Case No. U81,690), a divorcee, aged 49, was referred to the clinic on Feb. 24, 1942, because of menorrhagia and metrorrhagia of four months' duration. In 1934, following thyroidectomy for Graves' disease at a local hospital, she had a convulsion and was found to have tetania parathyreopriva. She was satisfactorily treated with parathormone (0.5 c.c. every other day), calcium, vitamin D, and thyroid substance. Although she had occasional paresthesias, no further convulsions or cramps occurred. She entered this hospital three weeks ago on the Gynecological Service, where uterine fibroids were discovered and a diagnostic curettage was done. The pathologic report has not yet been issued. In order to produce an artificial menopause 1,500 millicuries of radium were inserted. When Dr. Brainerd saw the patient in consultation, he noted coarseness of hair, dryness of skin, and bilateral 2 + Chvostek and Trousseau signs. The patient had hypochromic anemia, with hemoglobin of 56 per cent. Her basal metabolic rate was −23 per cent. Chemical studies of the blood gave the following results: Feb. 25, calcium 7.26 mg. per 100 c.c., phosphorus 5.95 mg. per 100 c.c.; Feb. 27, cholesterol 208 mg. per 100 c.c.; March 13, calcium 8.44 mg. per 100 c.c., phosphorus 6.87 mg. per 100 c.c.; March 17, phosphorus 5.84 mg. per 100 c.c.

The patient was placed on high-calcium, low-phosphorus intake with parathormone (50 units daily), vitamin D, hydrochloric acid, and lactose. Twelve hours after discharge marked angioneurotic edema of the mouth, larynx, and vulva developed. The patient was seen on the Medical Service in active tetany. This was controlled with adrenalin, ephedrine, and calcium given intravenously. The angioneurotic edema probably was precipitated by codeine and aspirin. There had been no previous attacks and thus far has been no recurrence. When Dr. Lisser saw the patient, he substituted dihydrotachysterol for the parathormone. Thereupon the calcium rose and the phosphorus also showed slight elevation. The Sulkowitch test[1] showed constant spillage of a small amount of calcium in the urine.

The patient has been maintained on 2 c.c. dihydrotachysterol daily. She has received 12 c.c. in a week's time. This dose will be reduced to 3–5 c.c. per week as soon as possible. A test taken yesterday (March 17) showed some reduction of blood phosphorus, although it is still abnormally high; the calcium has not yet been reported.[2] Today the patient demonstrates evidence of old thyroidectomy. Her Chvostek and Trousseau reactions are negative. Her skin is dry; her eyes are somewhat puffy; her teeth are in fair condition; her nails are brittle; she has no visible cataracts and no carpopedal spasm.

PARATHYROID DISEASE IN CHILDREN

Dr. Francis Scott Smyth

Perhaps the pediatrician approaches the subject of parathyroid disease primarily through his early interest in rickets. We now recognize that many conditions in which demineralization of the skeleton occurs may be accompanied by hypertrophy of the parathyroids. It is not always possible to have a clear-cut picture of hyperfunction or hypofunction. Many of our problems in differential diagnosis are those in which the x-ray appearance strongly suggests parathyroidism but is not necessarily due to adenoma.

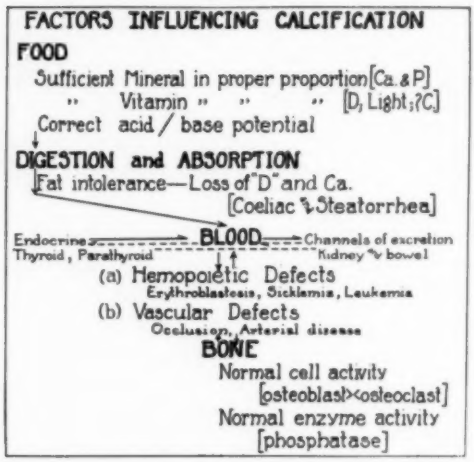
For years pediatricians have been con-

[1] Sulkowitch reagent: Oxalic acid 2.5 gm., ammonium oxalate 2.5 gm., glacial acetic acid 5.0 c.c., distilled water q.s.a.d. 150.0 c.c.

[2] Ca, March 17, 1942, 9.56 mg. per 100 c.c.

cerned with the growth of the skeleton and with defects that may be encountered in cases of faulty intake of calcium, of phosphorus, or of both, and of vitamin D (Table I). These, however, are not the

TABLE I



only factors. Demineralization may occur because of excessive acid. Excessive base intake may cause faulty absorption. The skeleton may be demineralized by a diet rich in calcium in proportion to phosphorus, or by the reverse. In treating certain types of demineralization, such as renal rickets and osteodystrophy, the unusually high phosphorus in the blood is somewhat counteracted by a diet excessively rich in calcium and base. We are concerned, however, not only with the intake of essential minerals, but also with their utilization, that is, their digestion. Due to faulty digestion loss of vitamin D and calcium may occur and may cause demineralization in certain diseases, such as steatorrhea. Sometimes the designation celiac rickets is used for this condition. These states naturally are more apparent in growing children, but even in adults with similar maldigestion, demineralization may occur. This morning we are primarily concerned with the factors that relate to the parathyroids. Here we must group the thyroid and parathyroid together although the functions of the two are different.

Our newer information leads us to suppose that the parathyroid hormone is able to shift the excretion of calcium. Normally about 70 per cent is excreted in the stool and 30 per cent in the urine. Under the influence of parathyroid extract experimentally, and in hyperparathyroidism clinically, these figures may be reversed, so that as much as 70 per cent may be excreted in the urine and the lower percentage in the stool. These observations have led us to investigate metabolism and, in the absence of other diagnostic features, such studies may be of great value. Whether the effect of the thyroid is due to an increase of metabolic gradient of the intestinal tract or to a shift of the calcium excretion has not been established. In the latter case the amount in the bowel is greater than normal. It may be as high as 80 per cent, while excretion in the urine is 20 per cent. In some instances hyperthyroidism in children is accompanied by demineralization. This may be due to an increase in metabolism, but there is considerable evidence that the thyroid itself, like the parathyroid, can affect the channel of excretion of these two minerals.

Dr. Aub has suggested a method for detecting excretion of calcium and phosphorus in the urine and stool.

NORMAL ADULT: DAILY AVERAGE CALCIUM AND PHOSPHORUS EXCRETION ON LOW-CALCIUM DIET

	Calcium	Phosphorus
Stool	0.20	0.12
Urine	0.063	0.41
Total Excretion	0.263	0.53
Intake	0.11	0.50
Balance	−0.153	−0.03
Blood	9–11 mg. per 100 c.c.	3–5 mg. per 100 c.c.

It is necessary to have the patient on a carefully weighed diet and to see that the correct acid-base potential is present, that serum proteins are normal, and that renal function is normal. The normal level of calcium in the blood is about 9–11 mg. per 100 c.c., that of phosphorus 3–5 mg. per 100 c.c. There is a preponderance of calcium in the stool. The negative balance of excretion over intake is about 0.153.

The Aub study is artificial because on this diet the patient receives not even a maintenance intake of mineral. This is done so that the finer changes may be detected which would be absent if a diet liberal in these minerals were given. The method is valuable in studying patients who may have hyperthyroidism or hyperparathyroidism.

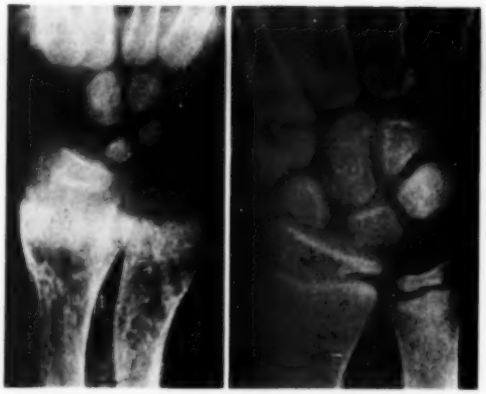
CASE 1: A girl, N. V., 5 years of age, showed the classical picture of rickets, but the problem was much more grave than that of infantile rickets because we were unable to obtain results with the average therapeutic doses of vitamin D, large amounts of bone salts, and the usual diet. X-rays (Fig. 1) showed, in addition to epiphyseal enlargement, a ground-glass appearance of the bone.

CASE 1: CALCIUM AND PHOSPHORUS EXCRETION ON AUB LOW-CALCIUM DIET (DAY PERIOD)

	Calcium	Phosphorus
Urine	0.0168	0.4780
Stool	0.3200	0.5050
Total Excretion	0.3368	0.9830
Intake	0.1870	1.2840
Balance	−0.1498	+0.3010
Blood*	9.1–8.4 mg. per 100 c.c.	1.98–1.85 mg. per 100 c.c.

* This patient had also a high blood phosphatase: 19.9—25.

The channel of excretion was normal and the blood level of calcium was not greatly altered. The level of phosphorus, however, was very low. This condition is sometimes seen in parathyroidism but it is also seen in cases of nutritional rickets. A 5-year old child should have about 5 mg. of phosphorus per 100 c.c. of blood. Furthermore, this patient had a markedly elevated phosphatase. She presented no evidence by the Aub study of hyperparathyroidism and, despite the extremely low phosphorus, her condition pointed largely to nutritional lack of vitamin D and to rickets. We felt justified in pushing our therapeutics far beyond those usually recommended for a patient with infantile rickets and gave her up to 50,000 and at one time close to 100,000 units of vitamin D. During the rise of phosphorus, which



A. 7-11-35 B. 10-23-40

Fig. 1. Case 1: Severe nutritional rickets. A, before treatment, demonstrates the typical rachitic epiphyseal and metaphyseal bone ends, marked coarsening of the trabeculation throughout the shaft, and periosteal new bone formation. B, taken five years later, following treatment, shows return to normal.

was the therapeutic effect of vitamin D, the calcium dropped and the Chvostek sign appeared. This might be considered a case of tetany induced therapeutically. The amazing thing is that this child required tremendous doses of vitamin D over a long period of time. Concentrates of vitamin D may be used in so-called resistant rickets provided the level of blood phosphorus is watched closely; when it reaches 4 mg. per 100 c.c. the high dosage should be discontinued. I believe instances of hypervitaminosis D are invariably related to use of the vitamin in patients whose blood phosphorus is not below normal. The therapeutic result is reached when the phosphorus returns to approximately normal. If high doses of vitamin D are being used, they should then be reduced.

CASE 2: In this patient, L. M., we have another Aub study in which the channel was not reversed but a tremendous loss of calcium occurred.

We learned more from this case than from some with classical findings of adenoma of primary hyperparathyroidism. This patient had evidences of hyperthyroidism. In addition she had had a fracture which might have been due to

Fig. 2. Case 2: Marked osteoporosis with hyperthyroidism. Part of this osteoporosis is nutritional, and part of it is the result of disuse. This patient has a phobia for walking.

faulty mineralization. Following the trauma she had a phobia for walking and exercising so that she had to be carried into the ward on a stretcher. Furthermore, she refused to take dairy products, especially milk and eggs. She presented a nutritional

CASE 2: CALCIUM AND PHOSPHORUS EXCRETION ON AUB LOW-CALCIUM DIET (FOUR-DAY PERIOD, 12-16 TO 12-20-32)

	Calcium	Phosphorus
Stool	0.521	0.460
Urine	0.206	1.564
Total Excretion	0.721	2.024
Intake	0.424	3.448
Balance	−0.303	+1.424
Blood	9.3–9.5 mg. per 100 c.c.	4.6–4.6 mg. per 100 c.c.

as well as a psychiatric problem. She also had atrophy of disuse. At one time it was thought that she must have hyperparathyroidism because the x-ray pictures suggested it (Fig. 2). An attempt was made to dissect out the parathyroid but only lymph nodes were found. This case was not an example of great success in removal of an adenoma. The success of therapy was due to a combination of things. I cannot say what factor was the most important. Diet, physiotherapy, psychotherapy, and x-ray therapy to the thyroid —all were important.

Perhaps in children more frequently than in adults secondary parathyroidism associated with profound renal disturbance is seen. Classically these patients have a congenital defect in the urinary apparatus. The kidney is apt to show extremely low excretion of phthalein and marked retention of non-protein nitrogen. In time demineralization appears, which is thought to be due to lowered calcium because elevation of blood phosphorus is found. The patients also have profound anemia, a lemon color, hypotonia, and demineralization of bone. In some cases not only elevation of phosphorus but also considerable elevation of calcium is found. Although in these cases the classical hyperparathyroidism is not seen, evidence is sufficient to suggest that the parathyroids are not functioning normally. A diffuse hypertrophy of the parathyroids is present which should not be confused with adenoma of primary hyperparathyroidism. The worst thing to do is to attempt surgical removal of the parathyroids. They are not adenomatous. It is hard to prove that they are necessarily in hyperfunction. It is probably safer to assume that the stimulation of the parathyroids to oversecretion is brought about by their attempt to eliminate the markedly elevated phosphorus. The first action of parathyroid extract is to cause marked diuresis of phosphorus. In instances in which phosphorus cannot be excreted, demineralization may obviously be encountered. Elevation of both calcium and phosphorus with calcification of soft tissue occurs in an aggravated stage.

CASES 3 AND 4: We were fortunate in being able to study the case of V. F. One need not go beyond the 19.2 mg. calcium, 2.56 mg. phosphorus, and elevation of phosphatase to diagnose this case. We have a very good picture of the Aub study

in this example of primary hyperparathyroidism with reversal of the channel of excretion and marked increase of calcium. Possibly the only condition in which phosphatase is higher than in parathyroidism is in Paget's disease.

CASES 3 AND 4: CALCIUM AND PHOSPHORUS EXCRETION ON AUB LOW-CALCIUM DIET

	Calcium	Phosphorus
Case 3: V. F.		
Stool	0.1440	0.1703
Urine	0.3727	0.7027
Total Excretion	0.5167	0.8730
Intake	0.0929	0.7766
Balance	−0.4238	−0.0964
Blood*	19.20 mg. per 100 c.c.	2.56 mg. per 100 c.c.
Case 4: J. F.		
Stool	0.0480	0.2801
Urine	0.4302	0.7676
Total Excretion	0.4782	1.0477
Intake	0.1040	0.8480
Balance	−0.3742	−0.1997
Blood†	18.20 mg. per 100 c.c.	2.10 mg. per 100 c.c.

* Blood phosphatase, 33.2 units.
† Blood phosphatase, 10.3 units.

V.'s brother, J. F., presented the same metabolic picture. During the postoperative course, V. showed a tremendous drop in calcium.

DIAGNOSTIC FEATURES

Dr. Mayo H. Soley

Parathyroid disease, like other endocrinopathies, is most easily discussed after it is separated into hypo- and hyperfunction of the gland. Perhaps the commonest clinical feature of hypoparathyroidism is the history of a thyroidectomy and the finding of one or more scars on the neck. In other words, hypoparathyroidism usually is seen after thyroidectomy. The idiopathic type, however, also occurs. The clinical features of the disease include muscle twitching, spasm, states of tension, occasional convulsions and, as illustrated in the case of B. G., a woman who is now thirty-three years old, epileptiform convulsions in early life. They also include the typical tetanic state with contraction of the flexor muscles. The same condition can, of course, be brought on by hyperventilation. There also may be laryngeal stridor, especially at night. Patients usually complain of a sensation of numbness and tingling. It frequently starts in the right hand of those who are right-handed and in the left hand of those who are left-handed. Then it progresses to the other upper extremity, to the legs and is felt around the mouth. Gastro-intestinal disturbances are not uncommon. Anal spasm, pylorospasm, and a degree of atony of the bowel associated with belching and distention may occur. These disturbances are the chief complaints of B. G., although she has had two pectenotomies. Not infrequently cataracts occur; the eyes should be watched carefully for this development. In most of the severe cases of hypoparathyroidism, cataracts have developed at one time or another. In one of our patients the cataracts improved with adequate therapy for hypoparathyroidism and hypothyroidism. Occasionally they improve on administration of thyroid substance.

On physical examination the patient with hypoparathyroidism may show muscle twitching, spasm, frank tetany, positive Chvostek sign (elicited by tapping the facial nerve), and positive Trousseau sign. Another finding is the increased ability of the muscle to contract with a rather low galvanic current. The average patient with hypoparathyroidism will have contraction with about half the current necessary for muscle contraction in a normal subject. Laboratory studies show hypocalcemia, the calcium level being perhaps 5, 7, or 8 mg. instead of the normal of 9.5 to 12 mg. per 100 c.c. If it is below 7 mg. frank tetany is present except in patients like B. G. who have had the disease over a long period so that they have accommodated themselves to the great changes in calcium and phosphorus metabolism. In the case of B. G. it frequently is impossible to produce positive Chvostek and Trousseau signs even with hyperventilation when the blood calcium is as low as 5.5 mg. per 100 c.c. and the blood phosphorus as high as 6.5 mg. per 100 c.c. Tetany probably depends on the amount of diffusible calcium in the blood. Whenever calcium

and phosphorus determinations are made, it is wise also to do serum protein studies because the non-diffusible calcium is bound with the serum protein. If the serum protein is low, the bound calcium also is low. The calcium is almost always absent from the urine as demonstrated by the Sulkowitch test because the serum calcium levels are below the threshold for renal excretion.

Hypoparathyroid tetany may be differentiated from hyperventilation tetany by the history and by determination of calcium levels. Also certain phases of rickets enter into differential diagnosis. Patients with osteomalacia on the basis of insufficient calcium intake and absorption may show some of the signs of hypoparathyroidism, particularly tetany, but the phosphorus as well as the calcium is always low. The disease is rare even in pancreatic deficiency. Then there is the tetany caused by metabolic types of alkalosis which involve loss of acid ions due to diarrhea or vomiting, or due to the ingestion of basic ions, as in the treatment of peptic ulcer. Most of these conditions can be differentiated by the history. Furthermore, the Aub test mentioned by Dr. Smyth may be useful in differential diagnosis.

In hyperparathyroidism certain typical clinical features are present. One of the commonest symptoms is weakness with hypotonia of the muscles. There is not infrequently an initial story of nephrolithiasis (renal or ureteral calculi). If this occurs repeatedly, hyperparathyroidism should be suspected. Albright found that in a group of 87 patients with hyperparathyroidism 22 had renal calculi. Pains in the bones and pathological fractures are often presenting symptoms. Pains in the bones are not always explainable and may occur in the absence of fractures or tumors. There may be changes in cardiac rhythm from a slow rate to ectopic rhythms such as paroxysmal tachycardia. Dr. Goldman and I have a patient in common who had paroxysmal tachycardia and 13 fractures, all of which were caused by trauma. Finally he complained that his kidneys felt as though they were rubbing together. He had two attacks of colic from nephrolithiasis localized on the left side. On that side renal stones were found. I believe this man has hyperparathyroidism. With increase in excretion of calcium in the urine polyuria and sometimes dysuria occur. Occasionally parathyroid enlargement can be felt. In cases of hyperparathyroidism of long standing in which there has been tremendous demineralization of bone, fractures may occur with only slight trauma. Deformities of the bones of amazing degree are seen.

Among the laboratory findings in hyperparathyroidism are generalized osteoporosis, cysts, tumors, and fractures of the bone demonstrable by x-ray. Determination of blood calcium usually reveals a level of from 12.5 to 29 mg. per 100 c.c. Excess of calcium in the urine as measured by the Sulkowitch test is indicated by a thick, whitish, chalky precipitate. Together with increase of blood calcium, lowering of blood phosphorus usually takes place, to below 2.5 mg. per 100 c.c. In most cases the blood phosphatase is elevated. Renal calculi are seen by x-ray examination or are suggested by the indirect evidence of blood in the urine. Not infrequently a certain type of hyalin cast is seen in the urine. This looks very much like other hyalin casts except that with a certain stain it appears black. If the urine is acid, this cast cannot be seen.

Hyperparathyroidism must be differentiated from a number of conditions. The x-ray appearance simulates primary or metastatic carcinomatous conditions of the bones. Demineralization is not unlike that in osteomalacia, although the clinical features, except for the fractures, are totally different. Differentiation must also be made from senile osteoporosis, which does not have the clinical features associated with hyperparathyroidism, and from Paget's disease.

MEDICAL TREATMENT

Dr. Hans Lisser

Hyperparathyroidism: The treatment of this hyperfunctional endocrinopathy is

chiefly surgical, to reduce parathyroid activity. It consists in removal of one, or even two adenomas. Rarely this syndrome can be caused by true hypertrophy of all four glands; in such an event three glands should be extirpated and all but 200 to 300 mg. of the fourth. A normally sized parathyroid should be left *in situ*. By hypertrophy is meant an amount of parathyroid tissue 40 to 100 times normal; the individual cell volume swells or grows to about 125 times normal. The ultimate prognosis depends on the extent of renal damage. Even though the bone changes are reversed by removal of the hyperfunctioning adenoma, recovery will not take place if renal calcinosis is too far advanced. Therefore, fluids should be forced. Milk should be forbidden, so as not to increase the nephrocalcinosis. Albright has cautioned against complete removal of the tumor in severe renal insufficiency, in order to diminish the risk of dangerously severe postoperative tetany. This is not ordinary hypoparathyroid tetany, which is caused by too little parathyroid tissue and normal bone. It is a far more grave condition, in which the "hungry bones" suck calcium and phosphorus from the blood serum with alarming rapidity. Almost immediately after surgery "bone destruction ceases and bone formation proceeds at terrific speed with production of marked hypocalcemia and an increased hypophosphatemia" (Albright). Consequently, almost constant intravenous administration of calcium gluconate is imperative to combat this perilous crisis.

Hypoparathyroidism (tetany consequent to the inadvertent removal of two or more parathyroid glands in the course of performing subtotal thyroidectomy): Fortunately this type of postoperative tetany has become rare in this clinic because our surgeons have perfected an operative technic, skillfully skirting these important structures. Since this symptom complex is brought about by a low level of the calcium in the serum, the goal of therapy is to raise or restore this level to normal (10 to 11.5 mg. per 100 c.c.), without overdoing and thus producing hypercalcemia. Herewith follows a brief résumé, more or less in historical order, of the procedures which aim to accomplish this result. Some of them have become obsolete in view of newer, more effective methods.

(*a*) Intravenous administration of calcium gluconate: In acute outspoken tetany in which prompt relief is urgently required, 10 c.c. of a 10 per cent solution of calcium gluconate given intravenously will produce alleviation within half an hour to an hour. This is the treatment of choice for speedy action. The gluconate is preferred to calcium chloride even though the latter contains more calcium, because there is far less risk of tissue necrosis should even a minute amount of the solution escape from the vein; calcium chloride is exceedingly irritating.

(*b*) Oral administration of calcium: After the acute critical stage has been overcome and when a milder chronic form of tetany persists, calcium lactate may be given in large amounts, 10 to 55 gm. (not grains) daily. As a rule, it is well tolerated. It should be dissolved in very hot water, as comparatively little is absorbed if it is mixed with cold water. Occasionally large doses cause nausea and diarrhea. This can be prevented, as a rule, by adding dilute hydrochloric acid. If calcium is used orally merely as an adjuvant to A.T. 10 (to be discussed later), the following prescription is useful: 1 tsp. t.i.d. per cup of water diluted solution of 10 c.c. of a 30 per cent solution of calcium chloride. The chloride tends to make the patient slightly acidotic (Albright), which is desirable since alkalosis causes tetany and acidosis alleviates it.

(*c*) Parathyroid hormone was discovered in 1924 by Collip and by Hanson independently. Through the courtesy of Dr. Collip, then professor of biochemistry at the University of Alberta, Edmonton, Canada, Dr. Shepardson and I had the good fortune to treat the first case of postthyroidectomy tetany with parathyroid extract. Subsequently three parathyroid glands were identified in the removed

goiter. Severe tetany occurred and was promptly controlled within two hours by parathormone. For the first few weeks the results were excellent and the patient received no other treatment. We had the opportunity of following her and managed to keep her alive for a year. This was remarkable because at autopsy no parathyroid tissue whatever was found, despite a careful search of serial sections of the entire neck.

We soon discovered (what has since been confirmed by others) that parathyroid extracts lose their potency and the patient seemingly develops an immunity, so that larger and larger doses become necessary to maintain him free of symptoms and to keep the blood serum calcium at a normal level. Since antihormones have become fashionable, some have ascribed this peculiar "fastness" to antihormone production. It is curious that parathyroid extract loses its effectiveness in so specific a parathyroid deficiency, since, with the exception of rare instances of diabetics refractory to insulin and a rare "irreversible stage" of Addisonian crisis, hormones such as thyroid, insulin, cortin, estrogens, and androgens, continue to supplement efficiently in endocrinopathies in which they are lacking. Be that as it may, even 100 or 150 units daily of parathyroid hormone fail to suffice, so that treatment becomes both expensive and futile. Fortunately, with the discovery of a simpler, cheaper and more dependable calcium-raising agent it has been possible to dispense almost entirely with the use of parathormone.

(*d*) Thyroid substance: Dr. Shepardson and I and Dr. Aub of Boston have discovered independently that thyroid substance raises the serum calcium level. Since many cases of postoperative tetany also involve postoperative hypothyroidism, it is wise in chronic tetany to administer thyroid substance according to need and tolerance.

(*e*) Vitamin D: This derivative of irradiated ergosterol increases absorption of calcium from the intestine. Therefore, if calcium is given, it is advisable to prescribe vitamin D in conjunction. This may be given as cod-liver oil or any one of the numerous preparations that contain adequate amounts of vitamin D. However, there is almost no need for this treatment since the advent of A.T. 10.

(*f*) Dihydrotachysterol (A.T. 10): This photochemical derivative of ergosterol was introduced by Holtz of Berlin in 1934. It has been called A.T. 10 because it happens to be "anti-tetanic preparation No. 10." It has revolutionized the treatment of hypoparathyroid tetany, as it is the easiest, most pleasant, and most effective form of treatment available. It is potent orally. It greatly increases the absorption of calcium and the excretion of phosphorus, both of which are eminently desirable. It acts more like the parathyroid hormone than like vitamin D (Albright). It can be used for long periods of time without increase of dosage or development of tolerance. It is available under the trade name, Hytakerol[3]. The initial dose in acute tetany is 3 to 10 c.c. daily or, if given in capsules, 6 to 20 capsules daily, for several days. As soon as the acute period has been controlled and the calcium of the blood serum has reached normal level (which is easily determined by the Sulkowitch test), the dose is dropped sharply to maintenance amounts of 1 to 7 c.c. per week. The dose must be individualized according to the severity of the condition, and overdosage with consequent hypercalcemia must be avoided.

The Sulkowitch test is simple and cheap. Blood serum calcium and phosphorus determinations are expensive; also misleading if they are not performed in a reliable laboratory. Blood for calcium test should be withdrawn in a dry sterilized syringe as boiling in tap water does not exclude the calcium in the water. When equal amounts of Sulkowitch reagent and urine are mixed in a test tube, absence of any precipitate indicates a low blood serum calcium since the renal threshold for calcium is between 5 and 7.5 mg. per 100 c.c. of serum. If a fine white cloud appears immediately, a moderate amount of calcium is present and

[3] Manufactured by the Winthrop Chemical Co.

the level of calcium in the serum is in the satisfactory range. If the precipitate looks like milk, the danger of hypercalcemia is imminent.

(g) Diet: Theoretically, in hypoparathyroid tetany there should be a high intake of calcium and a low intake of phosphorus, but in practice this is best met by omitting milk. Milk is contraindicated although it has a high calcium content, because it likewise has a high content of phosphorus, which is undesirable.

SURGICAL ASPECTS

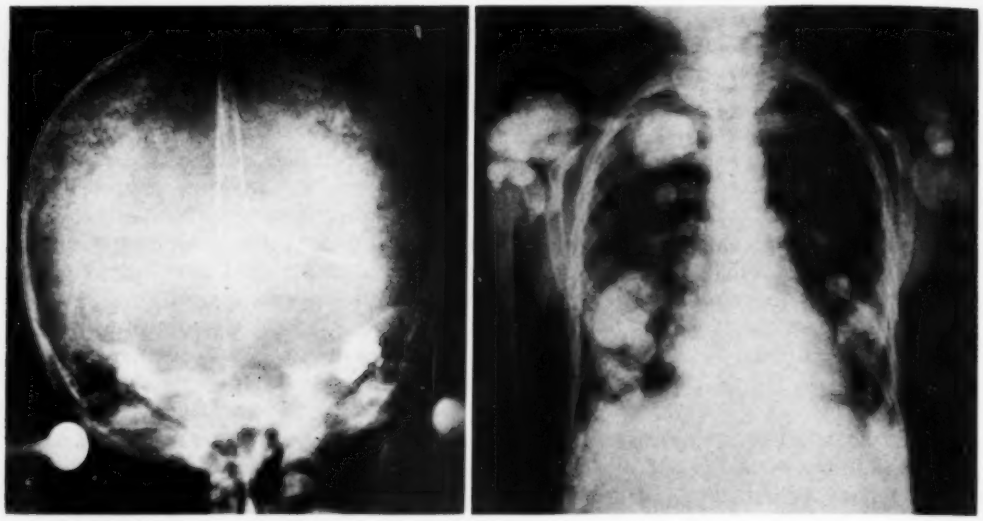
Dr. Leon Goldman

As has been said, most cases of hypoparathyroidism are the result of thyroidectomy. Although it has been known for a long time that the parathyroids are in a certain location in relation to the thyroid, Theodor Kocher was the first to become aware of their significance in producing tetany. Doctor Terry did much in devising an operation which, if carried out properly, will leave the parathyroids in good condition after thyroidectomy. He accomplished this by doing an intracapsular excision of the gland. In the development of a goiter the parathyroids are apt to be dislocated from their normal position, so that they may be found laterally or posteriorly. Therefore, the parathyroid bodies must be visualized at the time of thyroidectomy. With some experience the glands may be detected by their color. They have a brownish chocolate color and their own blood supply. At times it is difficult to differentiate them from small lymph nodes, from aberrant thymus tissue or from fetal adenoma or fat. After the thyroid has been removed, it should always be inspected for the possible presence of parathyroid bodies. If one is found, it should be removed from the thyroid tissue and implanted. Halsted found that if the need exists the tissue will probably grow. There is some controversy over the subject, but certainly no harm is done by carrying out such a procedure. Before thyroidectomy the patient should be tested for the Chvostek sign, since even in the absence of hyperventilation some patients have a positive reaction.

The first symptoms of post-thyroidectomy hypoparathyroidism which may be due to operative injury or removal of the parathyroids is paresthesia of the hands, the feet, and the perioral region of the face. If this occurs within twenty-four hours, the assumption may be made that parathyroid tissue has been removed or destroyed at operation. In patients in whom it is destroyed in healing of the wound, symptoms arise three or four days after the operation. If the symptoms come on early, they presage a rather grave injury. The next symptom after a positive Chvostek sign and paresthesia is spasm. We do not want the patient to go into convulsion. We always treat him, therefore, before it can develop. It is unusual for spasm or carpopedalspasm to develop if proper therapy is carried out.

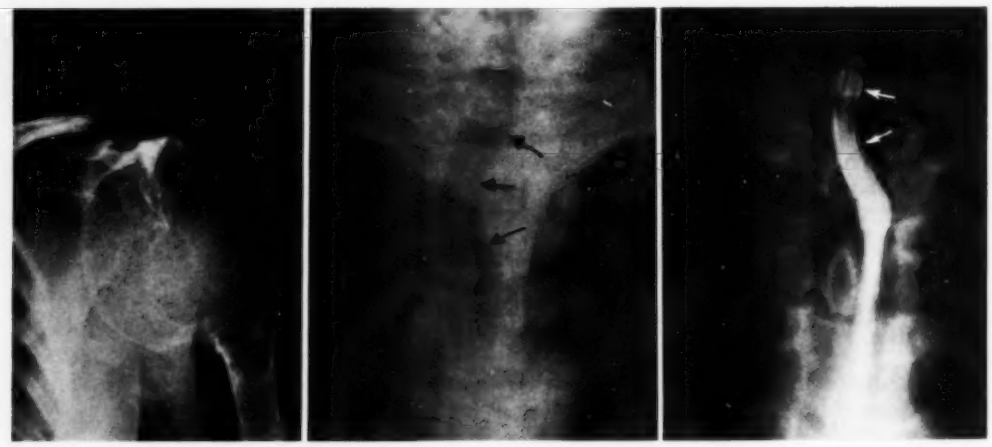
The treatment is as Dr. Lisser has outlined. We usually do not give all the substances mentioned immediately but try to carry the patient along on calcium, which should be given frequently. If that is sufficient we do not give thyroid substance immediately after operation since the latter was done to correct hyperthyroidism. Calcium should be given frequently even during the night, as it disappears from the blood stream in a short time. Patients who suffer carpospasm in the night often become depressed because they think they are paralyzed.

The recognition of hyperparathyroidism is not always as simple as some of the cases demonstrated might suggest. A typical case is easily recognized but because of the large group of patients with unclassified bone disease, it is often difficult to make a diagnosis. We prefer that it be made by laboratory tests rather than by exploratory operation, as the latter is difficult to carry out. The first operation presents the golden opportunity of finding a parathyroid tumor. If the patient has already been operated upon, the network of scar tissue makes exploration difficult. The



Figs. 3 and 4. The pebbly skull, with calcification of the tentorium and the falx, in a young patient with renal rickets, is quite typical of parathyroid overactivity. There was autopsy evidence of hyperplasia of the parathyroids.

The white areas in the soft tissues, in the same patient, are soft calcium soaps. They were found to be widespread throughout the soft tissues of the body. There is marked osteoporosis, with bending of the humeri, amounting almost to pathological fracture, especially on the left.



Figs. 5 and 6. Cases 3 and 4, in brothers: Fig. 5, on the left, shows a fairly typical cyst found in the bone in a case of true hyperparathyroidism (Case 3). The bone is expanded, and in this case trabeculated, though often these cysts are without trabeculations. They are very frequently multiple. In this particular case the osteoporosis distal to the cyst was due to disuse. The rest of the bones show relatively little osteoporosis. Frequently, even on biopsy, these are thought to be giant-cell tumors because of their appearance, location, and histology. Chemical studies of the blood are the most important point in differentiating them from true giant-cell tumors.

Fig. 6A (center) is also of Case 3. The arrows point to a deformity of the trachea due to pressure from the tumor of the parathyroid.

Fig. 6B (right) is of Case 4. It shows a similar deformity of the esophagus due to pressure the large parathyroid adenoma. Pressure symptoms from enlarged parathyroids are rare.

one who does the exploring should be thoroughly familiar with this region and with the various locations in which a parathyroid adenoma may occur. These are multiple. Therefore, the exploration must be complete. If no tumor is found, normal parathyroid tissue should not be removed. After removal of a parathyroid tumor, if there is a sudden drop in the calcium level (18–10 mg. per 100 c.c.), the symptoms of tetany may be due to the calcium depletion in the bones or to the atrophy of the normal parathyroid bodies that remain. Several days are required before normal parathyroid function will be resumed.

Parathyroid adenoma may be found in the substance of the thyroid gland. In one of our patients a calcium level around 19 dropped within six hours to about 10.5 mg. per 100 c.c. Symptoms of latent tetany with positive Chvostek and Trousseau signs developed. Symptoms may be produced in the same manner as in a sudden drop of blood sugar level in diabetes although this may still be above normal. The calcium level in this patient was finally controlled without medication.

A cyst of the tibia before surgery shows filling in with calcium deposit eighteen months later. A patient with parathyroid adenoma attached to the posterior capsule had no tetanic symptoms, probably because the skeleton had a good store of calcium.

X-RAY DIAGNOSIS

Dr. E. R. Miller

X-ray has little to offer in the diagnosis of hypoparathyroidism. In hyperparathyroidism the primary points in the x-ray diagnosis are osteoporosis, cyst formation, tumor production, and metastatic calcification of soft tissue. Marked osteoporosis may occur as in a case of renal rickets (D.R.). Here there was marked hyperplasia but no tumor formation in the parathyroids. The bones showed loss of calcium, thinning of the trabeculae, and a tendency to thinning of the cortex of the bone. The skull had a pebbly appearance

Fig. 7. Case 4: Lesion of the jaw thought to be a giant-cell tumor on roentgenologic study and on pathological section. This type of lesion occasionally occurs in a true hyperparathyroidism, as in this case (see Table, page 716).

(Fig. 3). Islands of normal bone were surrounded by areas of osteoporosis. That is the typical skull of hyperparathyroid activity. This case was not associated with cyst or tumor formation in the bone. Calcification had occurred in the falx and the tentorium, which is very unusual in a young person. Marked osteoporosis was also seen in the phalanges with coarsening of the trabeculae. There were multiple areas of increased density throughout the soft tissues of the body (Fig. 4). These represent soft calcium soaps.

The films in the case of V. F. (p. 718) showed fairly typical cysts. The cysts in hyperparathyroidism (Fig. 5) are usually multiple, occur in tubular bones, expand the bone, and are almost always monolocular. They appear as sharply demarcated areas of decreased density devoid of trabecular pattern in an osteoporotic bone. The adenoma of the parathyroid exerted pressure on the trachea (Fig. 6A).

The tumor of the mandible in a fighter,

Fig. 8. Simple bone cyst. These cysts may or may not be trabeculated. They occur near the ends of long bones, but do not involve the epiphyseal lines. Their first symptom may be fracture. They are almost always single lesions without evidence of osteoporosis or hyperparathyroid overactivity. Their failure to involve the epiphyseal line differentiates them from giant-cell tumors.

J. F. (p. 719), was thought to be a giant-cell tumor from its roentgen appearance (Fig. 7) and from biopsy. It was treated with x-ray. Later we learned that this patient was the brother of V. F. Investigation of the skeleton showed generalized osteoporosis and cysts and pressure on the esophagus (Fig. 6B) from the parathyroid adenoma.

Conditions to be considered in differential diagnosis from the x-ray point of view are almost legion. On the one side are the cystic lesions in bone, the simple bone cysts (Fig. 8). These usually present no symptoms until a fracture occurs and are found mostly in the upper ends of the humerus and tibia. They usually occur in young persons. They are single lesions, usually with some trabeculation, unassociated with generalized skeletal demineralization and thereby can be differentiated from the hyperparathyroid cyst. Prognosis in these cases is excellent. The lesion heals readily after fracture or curettement.

Another lesion that must be differentiated is regional cystic disease, so-called osteitis fibrosa disseminata. It may affect one extremity or one side of the body.

Fig. 9. Giant-cell tumor. Giant-cell tumors are expanded lesions at the ends of long bones, usually occurring in adults whose epiphyses have closed. The lesions appear as areas of decreased density crossed by coarse trabeculation. There is no chemical evidence of hyperparathyroidism. The lesions are always single.

In the case illustrated (Figs. 10 and 11) the left hand and foot were involved, with changes especially in the 2nd metacarpal, 1st metacarpal, and in the proximal phalanx of the great toe. The entire left tibia and femur were involved, while the right tibia and femur were free of the disease.

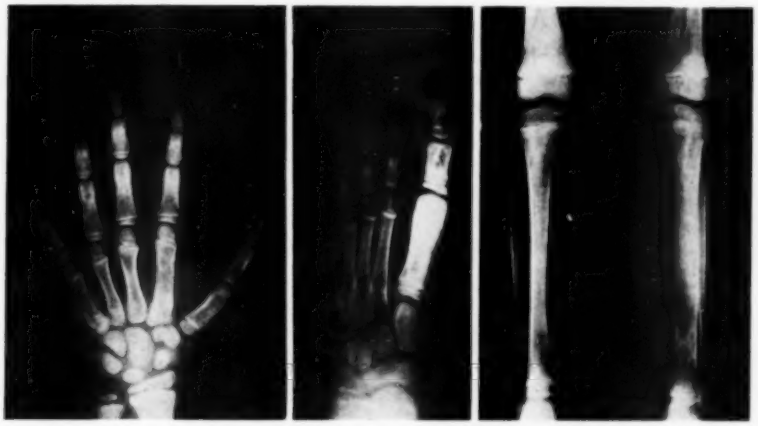
True giant-cell tumors also enter into differential diagnosis. These are single, trabeculated, cystic lesions (Fig. 9) which usually occur in the region of the epiphyseal line in a person whose epiphyses are closed.

Another lesion to be differentiated is

enchondroma, which is eccentric and cyst-like. It usually is seen in otherwise normal phalanges.

Paget's disease usually offers little difficulty in differential diagnosis because of the marked enlargement of the bone, its increased trabeculation, the thickening of the cortex, and the areas of increased and decreased density throughout the lesion.

Occasionally multiple myeloma causes difficulty in differential diagnosis. Other osteolytic tumors may resemble the cystic lesions of hyperparathyroidism. In these conditions, however, studies of serum calcium, phosphorus, and phosphatase of the blood, as well as biopsy studies, will determine the diagnosis.



Figs. 10 and 11. Regional osteitis fibrosa disseminata. These lesions usually involve half of the body, that is either the right or left side, or not infrequently the top half or lower half. The left hand and left foot are shown here. The right hand and right foot are normal. Similarly the left femur and tibia were involved, as shown, while the bones of the right extremity were normal. All lesions occurred on the left side of the body. Histological section shows this to be an osteitis fibrosa. Chemical studies of the blood showed no evidence of hyperparathyroidism.

PATHOLOGICAL ASPECTS

Dr. Stuart Lindsay

The normal histology of the parathyroid glands varies considerably, depending on age. Until the time of puberty, a parathyroid gland is composed entirely of chief cells. These have comparatively large, round nuclei with abundant chromatin and a relatively small amount of faintly eosinophilic cytoplasm. They contain glycogen and, after puberty, also fat. They are thought to be the cells that produce the glands' secretion. As the individual grows older, other cells begin to appear. These probably are altered chief cells. The water-clear cells have a clear cytoplasm and hyperchromatic, eccentric nuclei. Transitional water-clear cells are the transitional forms between the chief and the water-clear cells. Oxyphil cells, both pale and dark varieties, begin to appear after puberty. They are characterized by definite eosinophilic granules within their cytoplasm. The stroma of the gland contains fat cells after puberty.

In primary hyperparathyroidism, the lesion responsible for the elevated blood calcium and osteoporosis usually is a solitary chief-cell adenoma of one gland. In the two cases of primary hyperparathyroidism which we have seen in this laboratory, chief-cell adenomas were found. If enough sections are taken, a rim of remaining normal parathyroid tissue may be seen surrounding the adenoma.

In secondary hyperparathyroidism with severe renal disease (renal rickets), hyperplasia involving all the glands is found. In the literature these cases are reported as

showing either a chief-cell or a water-clear-cell hyperplasia. We have seen two such cases recently at autopsy. In one a mild water-clear-cell hyperplasia was found and in the other a very marked chief-cell hyperplasia. In the latter, one gland contained a true adenoma surrounded by a rim of less hyperplastic parathyroid tissue. In a recent autopsy of a 77-year-old male with Paget's disease, we found a moderate hyperplasia of all the parathyroids, involving all types of cells. In secondary hyperparathyroidism the clinical and laboratory findings are less easily correlated with the pathological changes than in the primary condition. Secondary hyperplasia has been described in a variety of primary osteolytic lesions as well as in renal disease.

Carcinoma of the parathyroid glands is rare. Only 18 cases have been reported in the literature. In only one case of this group was there any evidence of hyperparathyroidism. One patient has been seen at this hospital; he had no evidence of parathyroid hyperfunction.

Occasionally there may be difficulty in differentiating histologically the bone lesions of primary hyperparathyroidism (osteitis fibrosa cystica) and giant-cell tumors. In primary hyperparathyroidism giant cells frequently are found. The stromal cells, however, closely resemble ordinary fibroblasts, whereas in a giant-cell tumor the stromal cells usually have oval or round vesicular nuclei. These findings may help in differentiating the two processes. Furthermore, most pathologists take into consideration the clinical, laboratory, and x-ray findings before they arrive at a pathological diagnosis.

DISCUSSION

Dr. Kerr: I have seen two patients with hyperparathyroid adenoma in whom tetany developed postoperatively although the calcium level of the blood was 11 to 12 mg. per 100 c.c. One might discuss whether the sudden change in the functional level was responsible for the symptoms or whether the symptoms occurred because the parathyroid tissue remaining was atrophied and unable to function quickly. We have not paid enough attention to production of symptoms through changes in functional level. We have discussed patients with calcium of 5 or 6 mg. per 100 c.c. who had no symptoms of tetany when that level had existed for a long time, whereas under different circumstances the patient whose calcium level dropped to 11 or 12 mg. per 100 c.c. had symptoms.

The dangers of administering large amounts of vitamin D in patients with this disease as well as in those with chronic arthritis must be kept in mind. A few years ago a physician well along in years administered to himself 2.5 million international units of irradiated ergosterol daily for about seventeen days. The most remarkable symptoms developed, consisting in relaxation, hypotonia, polyuria, etc. Coma ensued and death occurred before renal stones and calcifications could develop in the tubules. The tissue showed large amounts not only of calcium but also of magnesium.

Question: Is the action of A.T. 10 cumulative?

Dr. Lisser: There is cumulative action when treatment is begun with large doses. Therefore, it is important to watch the calcium level in the urine by Sulkowitch test.

Question: Can the pathological findings in parathyroid disease be correlated with the clinical and chemical observations?

Dr. Lisser: Endocrinopathies may be severe clinically, with marked chemical disturbances, but without cytologic correlation. Notably is this true in the case of diabetes mellitus, in which, as a rule, pathological alterations in the islands of Langerhans may be negligible or not discernible.

In 1925 Dr. Shepardson and I had the opportunity of using parathormone in a patient suffering from severe maternal postpartum tetany. At first it was administered intravenously. We had gratifying success.

Idiopathic hypoparathyroid tetany, as illustrated by the case of B. G., has been

alluded to above. Autopsy in one such case, reported by Drake, Albright, Bauer and Castleman, revealed the extraordinary picture of four normal-sized parathyroid glands totally devoid of epithelial cells, which were entirely replaced by fat cells—a sufficient cause for lack of function.

The curious condition referred to by Doctor Miller as unilateral osteoporosis, confined to one side of the body, is associated with areas of pigmentation restricted to the same side. In girls this peculiar malady is accompanied by a remarkable sexual precocity. How these bizarre and seemingly unrelated phenomena can be tied together is perplexing. It is important to be aware of the existence of such a syndrome so that a parathyroid operation is not advised for a supposed hyperparathyroidism.

The same implication applies to the osteoporosis of disuse. Albright, Burnett, Cope, and Parson reported a remarkable instance of acute atrophy of bone (osteoporosis) simulating hyperparathyroidism. A boy of 14 had a fracture of the femur through a solitary bone cyst. Open reduction was performed and a cast was applied with immobilization from the waist down. Anorexia and vomiting followed due to hypercalcemia of 14.6 mg. per 100 c.c. The serum phosphorus and phosphatase, however, were normal. X-rays showed extreme decalcification of the immobilized parts of the skeleton without involvement of the other bones. The urine showed large amounts of calcium and many calcium phosphate casts. In view of the renal damage and the hypercalcemia, parathyroid exploration was twice attempted but failed to reveal adenoma or abnormal parathyroid tissue. Finally the clinical picture was correctly interpreted. The patient was mobilized and activity and weight-bearing were forced. In a month the serum calcium became normal, anorexia and vomiting ceased, renal function returned to normal, and the boy made an uneventful recovery.

Doctor Kerr has mentioned the occasional occurrence of tetanic symptoms when there is a sharp drop in the serum calcium even though it does not decrease to an abnormally low level. A comparable phenomenon has been observed by Doctor Shepardson and others in persons who become fatigued in the late afternoon. A glucose tolerance test will show a rapid uptake of sugar in the blood followed by a rather precipitate fall, but again not to a hypoglycemic level.

Dr. Kerr: In case of unilateral bone lesions, could a unilateral disease involving the adrenal or ovary on that side be responsible for the sexual precocity?

Dr. Lisser: We have seen a young girl who has unilateral osteoporosis, without pigmentation but with striking sexual precocity. One or more examiners claim to have felt a mass in her pelvis. We have advised exploratory laparotomy for a possible granulosa-cell tumor. If such were found, it would be interesting to observe whether its removal would have a favorable effect on the bone lesions.

REFERENCES

ALBRIGHT, F., BURNETT, C. H., COPE, O., AND PARSON, W.: Acute Atrophy of Bone (Osteoporosis) Simulating Hyperparathyroidism. J. Clin. Endocrinol. **1:** 711–716, September 1941.

ALBRIGHT, F., BUTLER, A. M., HAMPTON, A. O., AND SMITH, P.: Syndrome Characterized by Osteitis Fibrosa Disseminata, Areas of Pigmentation, and Endocrine Dysfunction, with Precocious Puberty in Females: Report of 5 Cases. New England J. Med. **216:** 727–746, April 29, 1937.

ALBRIGHT, F., SULKOWITCH, H. W., AND BLOOMBERG, E.: Hyperparathyroidism due to Idiopathic Hypertrophy (Hyperplasia?) of Parathyroid Tissue: Follow-up Report of 6 Cases. Arch. Int. Med. **62:** 199–215, August 1938.

ALBRIGHT, F., ET AL.: Effect of Phosphate Ingestion in Clinical Hyperparathyroidism. J. Clin. Investigation **11:** 411–435, March 1932.

ALBRIGHT, F., BAIRD, P. C., COPE, O., AND BLOOMBERG, E.: Renal Complications of Hyperparathyroidism. Am. J. M. Sc. **187:** 49–65, January 1934.

ALBRIGHT, F., BLOOMBERG, E., CASTLEMAN, B., AND CHURCHILL, E. D.: Hyperparathyroidism due to Diffuse Hyperplasia of All Parathyroid Glands Rather than Adenoma of One; Clinical Studies on 3 Such Cases. Arch. Int. Med. **54:** 315–329, September 1934.

ALBRIGHT, F., SULKOWITCH, H. W., AND BLOOMBERG, E.: Further Experience in Diagnosis of Hyperparathyroidism, Including Discussion of Cases with Minimal Degree of Hyperparathyroidism. Am. J. M. Sc. **193:** 800–812, June 1937.

ALBRIGHT, F., BLOOMBERG, E., DRAKE, T., AND SULKOWITCH, H. W: Comparison of Effects of A.T. 10 (Dihydrotachysterol) and Vitamin D on Calcium and Phosphorus Metabolism in Hypoparathyroidism. J. Clin. Investigation **7:** 317–329, May 1938.

ALBRIGHT, F.: Metabolic Effects of A.T. 10 Compared with Those of Vitamin D and with Those of Parathyroid Hormone. Tr. A. Am. Physicians **53:** 221–226, 1938.

ALBRIGHT, F.: Note on Management of Hypoparathyroidism with Dihydrotachysterol. J. A. M. A. **112:** 2592–2593, June 24, 1939.

ALBRIGHT, F.: Parathyroids: Physiology and Therapeutics. J. A. M. A. **117:** 527–533, Aug. 16, 1941.

BARR, D. P., AND BULGER, H. A.: Clinical Syndrome of Hyperparathyroidism. Tr. A. Am. Physicians **44:** 238–241, 1929; also in Am. J. M. Sc. **179:** 449–476, April 1930.

BARR, D. P., BULGER, H. A., AND DIXON, H. H.: Hyperparathyroidism. J. A. M. A. **92:** 951–952, March 23, 1929.

BARR, D. P., MACBRYDE, C. M., AND SANDERS, T. E.: Tetany with Microscopic Intracranial Pressure and Papilledema: Results from Treatment with Dihydrotachysterol. Tr. A. Am. Physicians **53:** 227–232, 1938.

BAUMANN, E. J., AND SPRINSON, D. B.: Hyperparathyroidism Produced by Diet (Low Calcium—High Phosphorus). Am. J. Physiol. **125:** 741–746, April 1939.

CAMP, J. D.: Roentgenologic Changes in Malacic Diseases of Bone. Radiology **26:** 399–408, April 1936.

CASTLEMAN, B., AND MALLORY, T. B.: Pathology of the Parathyroid Gland in Hyperparathyroidism. Am. J. Path. **11:** 1–72, January 1935.

CASTLEMAN, B., AND MALLORY, T. B.: Parathyroid Hyperplasia in Chronic Renal Insufficiency. Am. J. Path. **13:** 553–574, July 1937.

CHURCHILL, E. D., AND COPE, O.: Parathyroid Tumors Associated with Hyperparathyroidism: 11 Cases Treated by Operation. Surg., Gynec. & Obst. **58:** 255–271, February 1934.

CHURCHILL, E. D., AND COPE, O.: Surgical Treatment of Hyperparathyroidism Based on 30 Cases Confirmed by Operation. Ann. Surg. **104:** 9–35, July 1936.

CHUTE, R.: Clinical Aspects of Hyperparathyroidism with Special Reference to Urology. J. Urol. **41:** 762–772, May 1939.

DRAKE, T. G., ALBRIGHT, F., BAUER, W., AND CASTLEMAN, B.: Chronic Idiopathic Hypoparathyroidism; Report of 6 Cases with Autopsy Findings in One. Ann. Int. Med. **12:** 1751–1765, May 1939.

ELLSWORTH, R.: Diagnosis and Treatment of Parathyroid Underfunction. Internat. Clin. **3:** 27–45, September 1933.

GOLDMAN, LEON, AND SMYTH, F. S. Hyperparathyroidism in Siblings. Ann. Surg. **104:** 971–981, December 1936.

HALL, E. M., AND CHAFFIN, L.: Malignant Tumors of Parathyroid Glands. West. J. Surg. **42:** 578–586, October 1934.

HOLTZ, F.: Dihydrotachysterol: Modern Treatment of Parathyroid Insufficiency. J. Clin. Endocrinol. **1:** 453–458, May 1941.

HURXTHAL, L. M., AND CLAIBORNE, T. S.: Treatment of Tetany with Dihydrotachysterol (A.T. 10). New England J. Med. **220:** 911–916, June 1, 1939.

LISSER, H., AND SHEPARDSON, H. C.: Tetania parathyreopriva Treated with Collip's Parathyroid Extract. Endocrinology **9:** 383–396, Sept.–Oct. 1925.

LISSER, H., SMITH, R. K., AND SHEPARDSON, H. CLARE: A Case of Maternal Tetany Relieved by Parathyroid Extract (Collip). J. A. M. A. **88:** 461–463, Feb. 12, 1927.

LISSER, H., AND SHEPARDSON, H. CLARE: A Further and Final Report on a Case of Tetania parathyreopriva Treated for a Year with Parathyroid Extract (Collip) with Eventual Death and Autopsy. Endocrinology **13:** 427–454, September–October 1929.

SMYTH, F. S., AND GOLDMAN, LEON: Renal Rickets with Metastatic Calcification and Parathyroid Dysfunction. Am. J. Dis. Child. **48:** 596–616, September 1934.

CASE REPORTS

Leiomyoma of the Colon[1]

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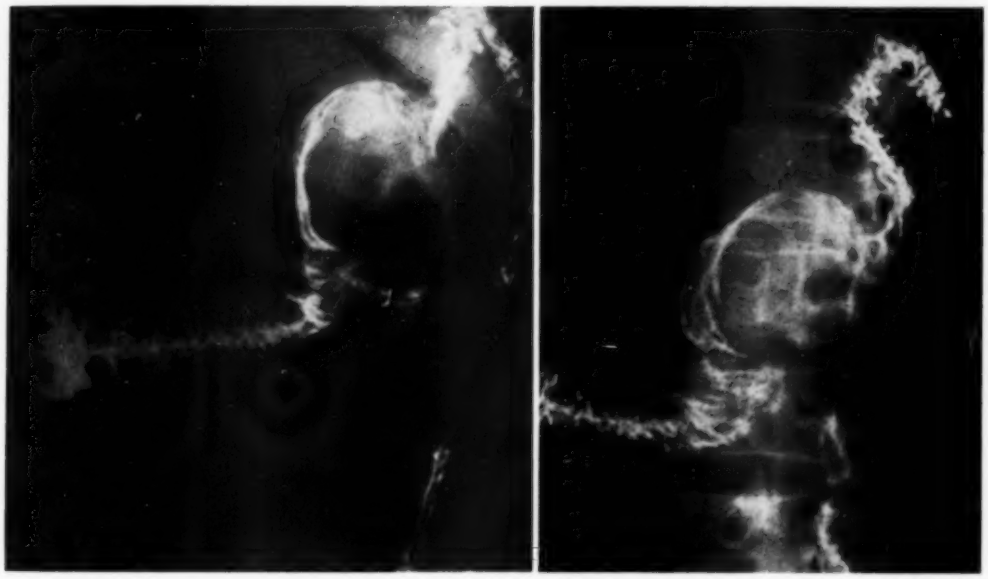
Tumors derived from smooth muscle occur in all segments of the gastro-intestinal tract. They are most common in the stomach and rarest in the colon. Of 28 leiomyomas and leiomyosarcomas, reports of which were collected by Geschickter, only 2 were located in the large intestine and both of these, one benign and one malignant, were found in the rectum.

The case report which follows is of interest, therefore, because of the rarity of the lesion. It is also of interest because, owing to certain roentgenologic characteristics, the histologic structure of the tumor was suspected before operation.

A man, forty-six years of age, registered at the Mayo Clinic on July 3, 1941, complaining of attacks of pain in the upper left portion of the abdomen. The first attack had occurred more than a year previously. The pain had been accompanied by a temperature of 102° F., a sensation of chilliness, and several watery stools. Relief followed a bowel movement or the passage of gas by rectum. In the three months prior to registration these attacks had become more frequent and the pain had become so severe that the patient was unable to walk upright. At no time was there nausea or vomiting and no blood had been observed in the stools.

Marked tenderness and rigidity of the abdomen, especially in the left upper quadrant, were noted on physical examination. Temperature by mouth was 99° F., and the pulse rate ranged from 78 to 88 beats per minute. No lesion was found in the rectum on proctoscopic examination. Laboratory studies brought out the following important facts: (1) the stools contained a large amount of pus, but no ova, parasites, or other organisms of significance; (2) the blood contained 28,300 leukocytes per cubic millimeter.

Roentgenologic examination of the chest showed the left side of the diaphragm to be elevated. The roentgenologic examination of the colon (Figs. 1 and 2) was reported as follows: "Tumefactive



Figs. 1 and 2. Leiomyoma deforming the transverse colon in the region of the splenic flexure. The mucosal relief pattern is preserved. The oblique view (right) shows the rounded deformity of the barium-filled lumen produced by the tumor.

[1] Accepted for publication in September 1942.

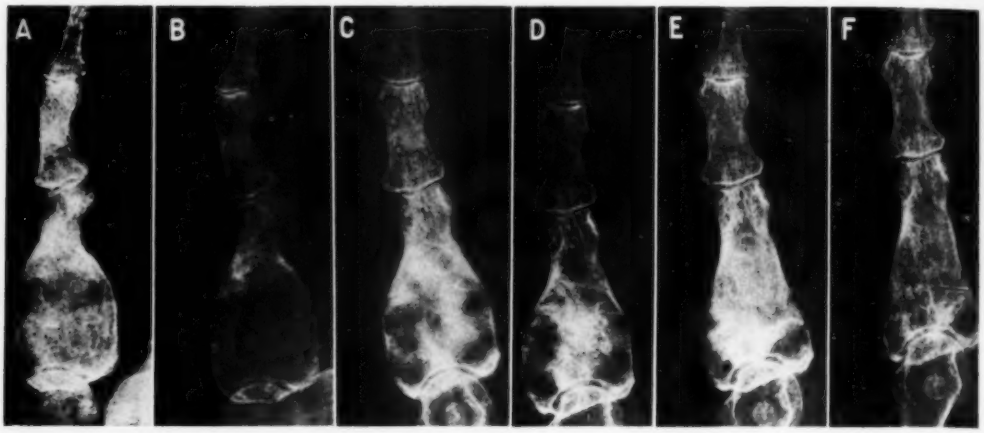


Fig. 1. Original cystic lesion of bone (A) and stages in the progress of healing. B. 1935. C. 1936. D. 1937. E. 1938. F. 1939.

lesion involving transverse colon near splenic flexure. Bowel is deformed in a semicircular manner. Mucosal aspect apparently preserved. Although exact nature of lesion is not firmly established, the findings are suggestive of intramural extraluminal tumor 6 cm. in diameter, such as leiomyoma, leiomyosarcoma, fibroma, or lipoma."

At surgical exploration Dr. C. W. Mayo found a tumor involving the transverse colon near the splenic flexure. It was adherent to the anterior abdominal wall, to the stomach, and to the jejunum. When opened, it contained foul smelling yellow pus. An extraperitoneal resection was done. The pathologist reported the tumor to be a degenerating, necrotic, infected, submucous leiomyoma of the transverse colon.

The roentgenologic characteristics of submucosal, intramural tumors arising in the small intestine have been reported previously (2). They are: (*a*) preservation of the mucosal relief pattern and (*b*) production of a rounded deformity of the barium-filled intestinal lumen by a mass which is firmly attached to the bowel. Such tumors are of many histologic types, among which are leiomyoma, fibroma, and lipoma. In our recent experience at the Mayo Clinic leiomyoma (including leiomyosarcoma) has been the most common.

As this case demonstrates, submucosal, intramural tumors of the colon produce the same roentgenologic features as their counterparts in the small intestine. Although the exact histologic nature of these tumors cannot be predicted by the roentgenologist, the intramural location can be demonstrated and the distinction from carcinoma can be made.

Mayo Clinic
Rochester, Minn.

REFERENCES

1. GESCHICKTER, C. F.: Tumors of the Digestive Tract. Am. J. Cancer **25:** 130–161, September 1935.
2. GOOD, C. A.: Tumefactive Lesions of the Small Intestine. J. A. M. A. **117:** 923–926, Sept. 13, 1941.

Bone Cyst Successfully Treated with X-Rays[1]

STUART P. BARDEN, M.D.
Philadelphia, Pa.

A case of a cystic tumor of a bone of the little finger, successfully treated, is of rather unusual interest because of the location of the lesion, the length of time it had been present (thirty years), its response to irradiation, and the control of pain by nerve section.

A. L. B., female, was first seen by us in June 1934. For the past thirty years she had had on the proximal phalanx of the little finger of the left hand a very slowly progressive swelling, which had re-

[1] From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania. Accepted for publication in August 1942.

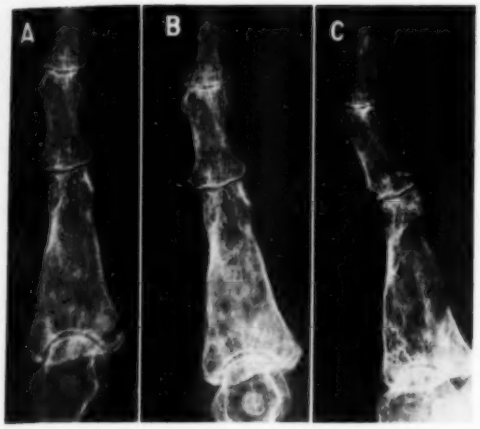


Fig. 2. Further stages in the progress of healing. A. 1940. B. 1941. C. 1942.

cently increased rapidly in size. Inspection of the part revealed a fusiform swelling of the finger, localized and covered by normal, non-adherent skin. It was moderately tender. Roentgen examination showed an expansile tumor of the proximal phalanx without any break in the cortex. Fluoroscopic examination of the skeleton at this time revealed no further bony lesions.

Roentgen therapy was instituted, and from June 13 to Sept. 6, 1934, the patient received 2,400 r measured in air directed over the part anteriorly and posteriorly. This was divided into four treatments of 600 r each. The factors were: *135 kv.p., 5 mm. aluminum filtration, 5 ma., 30 cm. target-skin distance, and 17 minutes time per treatment.*

Between the second and third treatments, the patient complained of so much pain in her finger that it became necessary to sever the sensory nerves to that area. This resulted in immediate and permanent relief of pain. We believe that this pain was *not* prompted by irradiation, but was due to the rapid increase in size of the lesion just prior to treatment, and was, therefore, merely coincident with the roentgen therapy.

The patient has been seen at least once a year since treatment. It was evident after a year that healing was progressing favorably. A roentgenogram taken on June 24, 1938, showed that the lesion was almost completely healed by bone, but that there was a fracture of the proximal end of the proximal phalanx, secondary to an injury sustained shortly before this examination was made. Subsequent yearly examinations showed healing of the fracture and further filling in of the tumor area with bone.

We have no biopsy of this lesion, but the appearance could be produced by either a bone cyst or a giant-cell tumor. Helwig has suggested that giant-cell tumors of long standing may be radioresistant; thus the long standing history of this lesion combined with the slow but steady response to irradiation we regard as evidence in favor of a bone cyst. The location, too, is uncommon for a giant-cell tumor, though this possibility cannot be entirely excluded.

Fig. 3. External appearance of lesion in 1934 (A), before treatment was begun, and in 1942 (B).

It is interesting to note that there has been very little in the American and British literature of the past ten years on irradiation of bone cysts. Almost invariably the treatment has been surgical.

It is recognized that cystic lesions of the bone often heal spontaneously after severe trauma to the lesion, as in surgery or accidental fracture. In this case, however, healing had been instituted *before* the fracture occurred. It is possible that the fracture contributed further to the favorable result.

3400 Spruce St.
Philadelphia, Penna.

REFERENCE

HELWIG, F. C.: Relative Importance of Histological Analysis in Tumor Therapy. Am. J. Roentgenol. **37:** 358–364, March 1937.

EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

Statistical Blunders

When one statistically minded reads a medical article, he does so with a foreboding, too often justified, that all is not well. A physician who has spent months or years accumulating data presents on them a statistical study that can hardly have occupied thirty minutes, and succeeds in proving only his own ignorance. In practically every instance the raw data are not published, so that a proper statistical analysis by others more informed on this science is impossible. The self-evident waste of effort and the folly of such tactics seem to elude many men engaged in clinical research.

A statistical analysis is, of course, dependent on a knowledge of mathematics and statistical methods, fields in which physicians are seldom well informed. Occasionally a physician has discernment enough to secure the help of a statistician, or sufficient interest to acquire a knowledge of the elements of statistics for himself; but this is exceptional. Yet surely the reader of an article purporting to prove a thesis by the analysis of a series of cases has the right to expect a clear presentation of the evidence, a fair analysis including consideration of the possibility that the chance variations of sampling may have influenced the result, and a conclusion which is clearly justified by the evidence offered. While it is not possible to discuss statistical methods in the scope of an editorial, some of the guiding principles can be mentioned, to indicate how one may achieve the desired standard.

The best time to begin work on the statistics is before beginning one's research, and the phase of the analysis then needed is the preparation of a *plan*. Helter-skelter assembly of data will never lead to a scientific proof of anything. Planned study has a reasonable chance of demonstrating the theory being investigated. The first part of a plan is the clear and precise statement of the problem to be studied. The second part comprises a statement of the method of study, including the designation of all factors on which figures are to be noted. And the final portion is the determination of how the conclusions are to be extracted from the raw data. In some instances an unplanned preliminary study may help the investigator formulate and define his final plan; but the final study must be clearly planned and precisely stated.

Having completed a plan, one may then proceed to gather figures. Although the medical profession seems in general to entertain the idea that the best way to do this is without plan, the fact is that unplanned samples are always biased, are seldom representative, and are never satisfactory. A sample is "random" in a statistical sense when an observed result, either success or failure, is completely unassociated with the method of choice employed in collecting the case, and the material chosen is a fair sample of the entire field of such cases. This often involves the most careful planning of the choice of cases for the sample. A sample not random in this sense is "biased," and will lead to more or less false conclusions depending on the degree of bias. Many doctors like to boast that they are presenting an "unselected" group. The mere fact that it is presented, however, proves that it was selected, or chosen, from all other similar

cases. It is much more to the point to give the criteria of selection. Were the cases all those seen between two certain dates? Were they all the cases in which adequate records were available? Were other criteria used? If a biased sample only is available, conclusions with allowance for this bias are sometimes offered; but this is an unreliable method which probably should not be employed. The figures gathered must be complete in all details. If for any reason complete details are not available, it is questionable whether the investigation is worth while.

While the sample should be large enough to permit a stable type of analysis, size in itself is no guarantee of the correctness of the conclusions. Thirty cases is often considered the minimum, but this statistical convention is not valid in every conceivable circumstance. The safest rule is, the bigger the better. The method of recording data is unimportant; the use of punch cards and sorting machines is convenient, but no more necessary than the use of an adding machine in calculating a sum. Accuracy and care are essential.

The sample may be analyzed by methods described in standard texts on statistics.[1] Choose the method that will give the desired information most readily and completely. The mere fact that one or another method has popularity in, say, the analysis of vital statistics does not prove it is best for your problem. If necessary, get a statistician to make this decision for you. But if possible do your own analyzing. The work of an outside statistician is seriously handicapped by ignorance of the medical intricacies of the problem. Don't hesitate to employ several methods of analysis independently; the work is often repaid by demonstration of your point.

Having analyzed your data, determine how dependable the results of the analysis are. *This is essential.* It involves determination of standard errors or of χ^2. Too often one sees major significance attributed to a 5 or 10 per cent difference when chances are good that this difference arose merely from sample differences. It is well to remember in this regard that statistical measures of reliability depend on an assumption of random sampling. If the sampling is not random—and much medical sampling is not—the measures are not strictly accurate. For practical purposes they are nearly so, but may be materially in error at times. Nevertheless, no statistical material should be published without the standard (or if you prefer, probable) error accompanying each important figure. This is especially true of differences between percentages (as cure rates, for example), whose entire significance is judged from the standard error.

In general, significance is the chance that a deviation has not arisen through the accidents of sampling, or the probability that an observation is not within the variability of a certain group whose variability is known. It is usually assumed that a variation of over three times the standard deviation is significant beyond question, since, given random sampling, the odds are 369 to 1 against such a variation being due to the chances of sampling. But even if a given variation fails to exceed three standard deviations, it cannot be said that it is meaningless; the probability that it has meaning is merely below that level at which it may be trusted. The standard deviation is the square root of the mean of the squares of the deviation of each observation from the mean. The probability of an occurrence differing from the mean by a given amount can be calculated by determining the number of standard deviations it lies from this mean, and comparing this with the corresponding area of a "normal" or Gaussian curve. χ^2 is a similar measure of probability, being calculated on the basis of the differences between each figure in the various compartments of a frequency table and the so-called "free frequency" or number which would have appeared if no associa-

[1] See, for example, Pearl, Raymond G.: Medical Biometry and Statistics, W. B. Saunders Co.; Fisher, R. A.: Statistical Methods for Research Workers, Oliver & Boyd, Edinburgh; Yule, G. Udny: An Introduction to the Theory of Statistics, C. Griffith & Co.; Ezekiel, Mordecai: Methods of Correlation Analysis, John Wiley & Sons.

tion between column and line existed. Comparison of the value calculated with tables based on theoretical calculations gives the probability of occurrence of such a value of χ^2.

It is important, also, to look for bias, since bias will distort the conclusions and invalidate the estimate of reliability. Careful comparison of the various groups, considering all factors and their distribution through the groups, is the only practical method for detecting bias. The groups need not be identical, but it is necessary that there be no segregation of cases by any factor which influences the result. Bias is often unconsciously introduced in that patients clinically worse have been given more energetic therapy, which tends to affect the experimental results. A full discussion of bias can be found in standard works on statistics.

The data and analysis must be presented in a form intelligible to a group of readers. You cannot expect your readers to guess at your data; you must present them fully, succinctly, and understandably. Just which data to present is often a problem to the medical writer. Should apparently irrelevant material be included, or not? It is usually best to give this material. Its negative value is considerable, and it may prove to have a positive value you do not suspect. If in any doubt at all, record it. In recording data, give all the facts for each case individually. If only two facts are recorded on each individual, a fourfold table will do; but ten fourfold tables do not give a complete record for twenty facts per individual; a twenty-column table would be required. Much time and space can be saved by a consideration of the form of presentation, since data usually may be condensed into tables or tabular summaries. In arriving at the conclusion that a given form is desirable, ask yourself the questions: "Does it give all the information so that another investigator could make a complete analysis from the facts supplied?" "Does it give it as briefly as possible?" A statement of a percentage of cures often appeals to the inexperienced as being all that is necessary; this is much too incomplete. In general, preference should be given to very brief case summaries or to a tabulation of cases in which each fact is tabulated for each case; more condensed forms are to be used with caution to supplant this, although they can helpfully supplement such a form. It is also wise to tabulate the results of analysis. Details must vary widely in accordance with the requirements of the problem; *the one really important thing is to be complete.*

Experimental research and clinical research have one basic difference; the experimenter can accurately control the experiment, while ethical and personal considerations usually prevent the clinician from making satisfactory control studies. The importance of proper controls is demonstrated repeatedly by articles purporting to prove this or that by reporting groups which are subsequently found not to differ significantly from a control group studied by someone else. This is the principal failing of the case report method of "research." If uncontrolled work is reported at all—it should seldom be—the conclusions must be most conservative. The fact that you *think* a procedure is helpful is not reason for omitting controls; you must *prove* the procedure's worth.

In presenting the conclusions, it is necessary to be clear, brief, and accurate. State what the data seem to show in as few words as possible. Note the points of agreement and disagreement with expectation, and offer any explanations that may account for the divergences. Indicate whether the figures seem to prove the conclusions beyond a reasonable doubt; if not, tell why. If the reason is a defect in the size or composition of the series, better tear up the article and start over again. And while conservatism is of the essence in interpretation, do not confuse it with the false modesty which prompts the making of an indefinite statement where a definite one is warranted.

A few don'ts to round off:

1. Don't state percentages without

giving the number of cases on which they are based.

2. Don't compare percentages or means without stating the standard error of the difference.

3. Don't use percentage comparisons at all when other methods (such as a table with calculation of χ^2 or a correlation analysis) are indicated for the problem in hand.

4. Don't use biased figures on which to base a conclusion.

5. Don't compare cure rates which have not all been calculated for the same follow-up period.

6. Don't omit the standard deviation or standard error of anything you calculate.

7. Don't forget: you *must* give the raw data, because no one can guess them from the results of your analysis.

8. Don't forget to *think*. It will save you from more blunders than any other procedure.

LEWIS G. JACOBS, M.D.

GENERAL LIMITATION ORDER ON X-RAY EQUIPMENT

A recent order issued by the War Production Board (General Limitation Order L-206, dated Oct. 20, 1942) is of special interest to radiologists. It is made necessary by defense requirements and the consequent shortage of materials entering into the manufacture of x-ray equipment. Under the latter heading are included fluoroscopic equipment and therapy equipment; power units; radiographic, fluoroscopic, and therapy tables; photo-fluorographic units; cassette changers; tube stands; stationary grids; Bucky diaphragms. Used or rebuilt equipment and parts, accessories or appliances used in connection with radiography, fluoroscopy, or therapy, other than the items specifically named, are not included.

Restrictions are placed both on the manufacture and sale of x-ray equipment. No manufacturer shall manufacture, continue the manufacture of, or assemble any models or types of x-ray equipment other than the permitted number of models of the types set forth in an appended schedule [see below].

No person shall sell, transfer, or deliver any x-ray equipment except:

(i) To the Army or Navy of the United States, the United States Maritime Commission and the War Shipping Administration, or

(ii) To persons (such as hospitals, medical departments of industrial concerns, and other persons desiring to receive x-ray equipment) who have filed a special application (Form PD-556) obtainable at the local offices of the War Production Board, and have been specifically authorized on such form by the Director General for Operations to receive x-ray equipment.

The form provides for statements as to the extent of x-ray equipment already in possession of the applicant, the number of patients per week on which the present equipment is used, and whether the desired equipment is for replacement purposes or is needed for expansion of existing facilities; also, as to how the work for which the equipment is desired is now being accomplished and what attempts have been made to obtain used or rebuilt equipment.

All persons affected by the order are required to keep and preserve for not less than two years accurate and complete records concerning inventories, sales, and deliveries, and to file such reports as may be required from time to time by the War Production Board.

Any person affected by the order who considers that compliance therewith will work an exceptional and unreasonable hardship on him may apply to the War Production Board setting forth the pertinent facts and the reasons such person considers that he is entitled to relief. The Director General for Operations may thereupon take such action as he deems appropriate. The order and all transactions affected thereby are subject to all applicable provisions of the Priorities Regulations of the War Production Board.

SCHEDULE A

Permitted Number of Models	Permitted Types	Description of Permitted Types
1	Power unit	Not to exceed 100 ma. at 90 kv.p. Self-rectifying, with mobile control
1	Power unit	Not to exceed 200 ma. at 100 kv.p. Full wave rectification, of a 2-tube design; either mobile or stationary control, or both
1	Power unit	1/2 microfarad condenser discharge
1	Power unit	Therapy unit, not to exceed 160 kv.p.
1	Power unit	Therapy unit, not to exceed 250 kv.p.
1	Dental x-ray unit	Wall model, not to exceed 15 ma. at 80 kv.p.
1	Dental x-ray unit	Floor model, not to exceed 15 ma. at 80 kv.p.
1	Vertical fluoroscope	Power unit not to exceed 15 ma. at 90 kv.p.
1	Portable unit	Power unit not to exceed 15 ma. at 85 kv.p. A portable unit is one that is easily disassembled and transported. It may be equipped with or without casters, and with either a collapsible or non-collapsible stand
1	Mobile or bedside unit	Power unit not to exceed 30 ma. at 90 kv.p. It is specially designed for moving on its own casters
1	Army field unit	Light duty, with a power unit not to exceed 15 ma., manufactured in accordance with the specifications of the Army of the United States
1	Army field unit	Power unit not to exceed 30 ma., manufactured in accordance with the specifications of the Army of the United States
1	Army tilting fluoroscopic unit	Light weight table, containing power unit not to exceed 15 ma. at 90 kv.p., manufactured in accordance with the specifications of the Army of the United States
1	Army field table	Manufactured in accordance with the specifications of the Army of the United States

1	Tilting table	Radiographic and fluoroscopic table, with or without mounting for fluoroscopic tube. The model may be hand-operated (hand crank or rocker) or motor-driven, or both
1	Stationary table	Horizontal Bucky table
1	Tube stand	Radiographic, with single column
1	Tube stand	Superficial therapy, with single column
1	Tube stand, or other support	Deep therapy. (The manufacturer may choose either a tube stand or any other type of support, but not both)
2	Cassette changer	Vertical or horizontal, with or without Bucky diaphragm
1	Stationary grid	Size 14 × 17″; either flat or curved, with focal film distance of 36″ if flat, or 43″ (plus or minus 1″) if curved; grid ratio 5 to 1; 50 lead strips per inch
1	Stationary grid	Size 17 × 17″; with focal film distance of 36″; grid ratio 5 to 1; 50 lead strips per inch
1	Stationary grid	Size 12 × 16″; with focal film distance of 30″; grid ratio 5 to 1; 50 lead strips per inch
1	Bucky diaphragm	Size 17 × 17″; with focal film distance of 36″; grid ratio 5 to 1; 50 lead strips per inch. May be constructed for either portable or table mounting
2	Photo-fluorographic unit	

NEBRASKA RADIOLOGICAL SOCIETY

The new officers of the Nebraska Radiological Society are A. F. Tyler, M.D., of Omaha, President, and F. L. Simonds, M.D., also of Omaha, Secretary-Treasurer.

LETTER TO THE EDITOR
A CORRECTION

To the Editor of RADIOLOGY:

In the next issue of RADIOLOGY will you kindly make the following correction of errors in my paper on Radium Poisoning published in July (Vol. 39, pages 39–47):

On page 44, in the fourth line from the bottom of the second column, the words "about 2 micrograms" should read "about 1.2 micromilligrams."

It should also be noted that the method used in computing the radium content of the bone was not a photographic method, as there stated, but an analytic method in which the electrometer readings are recorded photographically, as described in the *Review of Scientific Instruments* 6:99–112, 1935.

Yours truly,

ROLLIN H. STEVENS, M.D.

In Memoriam

HAROLD H. WEBB, M.D.

1890–1942

Word has been received of the death, early in November, of Dr. Harold H. Webb of Ottumwa, Iowa. Doctor Webb was born in New Castle, Va., and was graduated in medicine from the University of Maryland in 1912. He engaged in general practice in Virginia, Tennessee, and Pennsylvania, and for the past ten years had practised his specialty in Ottumwa. He was a diplomate of the American Board of Radiology and a member of the American College of Radiology and the Radiological Society of North America.

Book Review

STANDARD RADIOGRAPHIC POSITIONS. By NANCY DAVIES, M.S.R., AND URSEL ISENBURG, M.S.R. A volume of 136 pages with 103 illustrations. Published by The Williams & Wilkins Company, Baltimore, 1941. Price $2.00.

This is the third book that has appeared in recent years on the subject of positioning in radiography. Written by two British technicians, with a foreword by S. Gilbert Scott, it presents in concise form the usual standard positions, illustrated by simple line drawings. The book is pocket size and easily consulted.

The drawings are not as instructive as they could have been if the surface anatomy rather than the skeleton had been used to illustrate positioning. There are also certain glaring deficiencies, such as the omission of lateral views of the shoulder, positions to show the tendinous insertions of the humerus, oblique views of the ankle, and others. Likewise, there are errors, such as the admonition to stop respiration in making postero-anterior views of the sternum with the tube eccentric. The book is inexpensive, easy to consult, and most of the statements are substantially correct. Nevertheless, more detailed books on technic are preferable.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse, N. Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association.—Secretary, J. T. Murphy, M.D., 421 Michigan St., Toledo, Ohio.

ARKANSAS

Arkansas Radiological Society.—Secretary-Treasurer, J. S. Wilson, M.D., Monticello. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Joseph D. Coate, M.D., 434 Thirtieth St., Oakland.

Los Angeles County Medical Association, Radiological Section.—Secretary, Donald R. Laing, M.D., 65 N. Madison Ave., Pasadena. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, Earl R. Miller, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School); second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Edward J. Meister, M.D., 366 Metropolitan Bldg. Meetings third Friday of each month at the Denver Athletic Club.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Acting Secretary, Walter A. Weed, M.D., 204 Exchange Building, Orlando.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, Warren W. Furey, M.D., 6844 S. Oglesby Ave. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Fay H. Squire, M.D., 1753 W. Congress St., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, M.D., Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Sydney E. Johnson, M.D., Louisville City Hospital, Louisville. Meeting annually in Louisville, third Saturday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society.

Shreveport Radiological Club.—Secretary-Treasurer, W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, E. M. Shebesta, M.D., 1429 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, Arthur B. Smith, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of each month except June, July, August, and September, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, F. L. Simonds, M.D., 1216 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Maurice Pomeranz, M.D., 1120 Park Ave., New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., 707 Race St., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport. The Society meets annually.

The Philadelphia Roentgen Ray Society.—Secretary, Robert P. Barden, M.D., 3400 Spruce St., Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Reuben G. Alley, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston Meeting in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, L. W. Baird, M.D., Scott and White Hospital, Temple.

VIRGINIA

Virginia Radiological Society.—Secretary, Charles H. Peterson, M.D., 603 Medical Arts Bldg., Roanoke.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russell F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Section on Radiology, Ontario Medical Association.—Secretary, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. D. Irvine, M.D., 540 Tegler Bldg., Edmonton, Alberta.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

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THE HEAD AND NECK

Intracranial Tumors in Children: Preliminary Study of 100 Cases. Wm. A. Smith and E. F. Fincher. Southern M. J. **35:** 547–553, June 1942.

Of 87 verified brain tumors in a series of 100 cases in children from 13 months to 15 years of age, 63 per cent were subtentorial and 86 per cent were gliomas. Besides the gliomas there were 5 cases of suprasellar cyst, 3 of sarcoma, 2 of hemangioblastoma, and 2 of meningioma. Duration of symptoms varied from three weeks to five years. The greatest incidence occurred between the ages of three and ten. The clinical progression had no very evident relationship to the histologic typing. The outstanding symptom was vomiting, which was sooner or later observed in 94 per cent of the cases. Visual disturbances came next in importance, choked discs having been observed in 55 cases. Headache was not so common as is generally supposed.

The medulloblastomas showed the highest operative mortality rate and the shortest average period of survival of all the posterior fossa tumors. There was, however, one ten-year survival in this group following decompression, biopsy, and irradiation. In 16 astrocytomas of the cerebellum, no operative deaths were encountered and good results were observed in several cases following repeated operation. In 6 cerebral astrocytomas treatment was less successful, though the survival period was longer than in the medulloblastoma group. Ependymomas present a more difficult surgical problem and have a lower survival rate, though better than the medulloblastomas. Craniopharyngiomas are difficult of diagnosis, and treatment whether by surgery or radiation is unsatisfactory. Meningiomas are rare in children. Of 2 cases encountered, one was successfully removed, but a right homonymous hemianopsia persisted. Death occurred postoperatively in the other, where a tumor weighing 156 grams was encountered with severe bleeding and compression of the brain.

Photomicrographs, roentgenograms, and a bibliography are included. MAX MASS, M.D.

Meningiomas. A. Jentzer. Schweiz. med. Wchnschr. **72:** 581–586, May 30, 1942.

Meningiomas constitute about 15 per cent of cerebral tumors. They behave as benign growths, with little tendency to recurrence. They are usually solitary and encapsulated, displacing the brain without invasion. Most of them are connected with the dura. The author divides these growths into 5 groups: (*a*) angioblastic meningiomas (Cushing-Bailey type); (*b*) multiple meningiomas; (*c*) locally recurring meningiomas (Petit-Dutaillis type); (*d*) meningiomas with local recurrence and metastasis; (*e*) infiltrating meningioma.

The angioblastic meningiomas arise from meningioblasts. They occur in the cerebellum, and are to be distinguished from vascular anomalies. They are characterized by cavernous blood sinuses, and their removal is usually accompanied by gross uncontrollable hemorrhage. Survival is rare.

Multiple meningiomas constitute 3 to 4 per cent of all meningiomas. Individually the lesions are surgically curable, but their multiplicity militates against success. As many as 100 lesions have been recorded in a single case. They are often associated with tumors of the nerve axes.

Locally recurrent meningiomas are rare, but may occur, with a greater or lesser interval. Metastasizing lesions are even less common.

While the tumor is originally contained in the cranial cavity, in many instances it ruptures its capsule and invades the surrounding structures, especially the calvarium. The signs produced by invasion are progressive erosion of the inner table, fine perpendicular lines of new bone radiating from the skull, hyperostosis palpable externally, and thickening of the vault. Intracranial hypertension leads to a dilation of the venous channels. Local calcification of the tumor may occur.

Meningiomas may occupy any part of the cranial cavity; they favor the frontal region somewhat. Clinical symptoms and signs are seldom sufficient for localization; ventriculography is necessary, as a rule. The signs, both clinical and radiological, may mimic other conditions.

Operative removal may be easy or hard. The isolation of a vascular pedicle has not proved helpful, and the greatest hazard is hemorrhage. The procedure suggested is the removal of a bone flap, which is sterilized in an autoclave for thirty minutes at 120° while the intracranial portion of the tumor is removed. The open dura is closed with a graft of fascia lata and the sterile bone returned over it and fastened with a bronze nail. These points are illustrated by 4 case reports; all these patients are still living, the longest survival to date being two and a half years.

LEWIS G. JACOBS, M.D.

Congenital Lacunar Skull ("Lückenschädel"). H. F. Bettinger. M. J. Australia **1:** 526–529, May 2, 1942.

"Lückenschädel," a peculiar condition of the skull observed in the newborn, is characterized by defects in the vault which vary considerably in size, shape, and number. They occur in the form of shallow depressions or deep cavitations, and often penetrate through the bone until only a membrane of dura and periosteum remains. The defects, lined by smooth, thick ridges of bone, are most commonly seen in the frontal and parietal regions. They are practically always associated with some disturbance of occlusion of the medullary canal, mostly in the form of spina bifida with meningocele.

The literature on congenital lacunar skull is briefly reviewed, with references, and a case in an infant dying at seven days is presented, with autopsy findings. There were associated skeletal deformities in the feet, which were in extreme talipes position, and in the spine. Two roentgenograms of the skull are reproduced, and the author calls attention to the typical nature of the roentgen picture, recalling that Maier (Radiology **23:** 615, 1934) was able to make a diagnosis from films taken before delivery.

Three questions as to pathogenesis are raised and thoroughly discussed: (1) Is lacunar skull a manifestation of general disease? (2) Is it a disturbance of the local ossification process? (3) Is it due to intracranial pressure, and if so, what is the mechanism?

The author believes that the development of lacunar skull is dependent upon a physiological incongruity between the skull and the brain toward the end of pregnancy. Under normal conditions, the cerebrospinal fluid, acting like a water cushion, ensures an equal pressure on all parts of the cranium. In cases of meningocele, however, the cerebrospinal fluid will escape into the sac and the brain will come into direct contact with the inner surface of the vault. Additional space for the growing brain cannot be obtained by bulging of the non-osseous parts of the cranium because the amniotic fluid around the skull obviates all pressure differences. Erosion of the bone by pressure atrophy will therefore occur wherever the gyri press most closely against the inner table, with production of a typical lacunar skull. DONALD R. LAING, M.D.

THE CHEST

Symposium on Tuberculosis. Schweiz. med. Wchnschr. **72:** 685–721, June 27, 1942. **Investigation on the Epidemiology of Tuberculosis in Denmark.** Th. Madsen, pp. 685–686. **Late Primary Tuberculosis and Its Developmental Tendencies.** W. Löffler, pp. 686–701. **Late Primary Tuberculosis and Its Early Evolution.** E. Uehlinger, pp. 701–708. **Late Tuberculous Primary Infection and Its Development.** S. J. Leitner, pp. 711–713. **A Severe Tuberculous Family Infection.** A. Wernli-Hässig, pp. 713–716. **Prognosis in Pulmonary Tuberculosis.** J. Stephani, pp. 716–717. **Temperature Fall After Sulfanilamide as a Differential Sign, Especially with Reference to Tuberculosis.** J. L. Burckhardt, pp. 717–718. **Diagnostic Errors in Tuberculosis and Other Matters.** E. Bachmann, p. 719. **Reporting of Tuberculosis, Especially in Retrospect, in Defense Workers.** E. Bachmann, pp. 719–721.

In *Madsen's* discussion of the epidemiology of tuberculosis he mentions, without amplification, the use of fluoroscopy and photofluorography for case finding.

Löffler presents a profusely illustrated article on the evolution of primary tuberculosis. He divides the discussion into five phases: (1) the primary period in adults in general; (2) the primary complex in malignant dissemination; (3) the primary complex in erythema nodosum; (4) the primary complex in exudative pleurisy; (5) the primary focal infection of adults.

(1) The first period may be characterized by an acute infiltrating form of disease commonly mistaken for a secondary manifestation. Clinically, the primary period may be two-faced, progressing to a certain point and from there either going through a benign reversible course or a malignant, irreversible one. The condition is primarily a hilar gland tuberculosis. Two signs permit one to be certain it is primary: a change from negative to positive in the v. Pirquet test and a change from a bipolar soft tissue shadow to a similar calcified one. The most usual localization of this type of the disease is in the right base, with the left mid-lung field next in frequency.

(2) The second group comprises cases of miliary tuberculosis and tuberculous meningitis. In these a primary complex can be found at autopsy, and generally on roentgen examination, although tomograms may at times be required for this purpose.

(3) Erythema nodosum is a typical manifestation of primary infection. It occurs more rarely in the course of a protracted secondary infection, and very rarely in tertiary phthisis. It is not correct, however, to state that erythema nodosum occurs in every case of primary infection.

(4) Exudative pleurisy, especially in young adults, is often the first sign of primary infection. It develops more or less rapidly following the development of the primary complex. This complication may occur in secondary or tertiary phthisis also.

(5) Primary focus tuberculosis in adults follows a basically different course from secondary or infiltrative tuberculosis, but it exhibits stages of resorption, induration, or bronchogenic dissemination. This course is not readily differentiated from that of secondary infiltration or early infiltrate.

In general, there is no sharply defined picture of primary infection tuberculosis; the condition leads to a heterogeneous picture. Some cases may produce roentgen changes only.

Uehlinger discusses the pathological development of late primary infections. The increasing occurrence of this condition is due to the decrease in the proportion of infections in childhood. In healthy populations, infection of 50 per cent is now to be expected in the 20 to 55-year age group. The significance of the late primary infection is obvious from the fact that it was found to be the source of 60 of 72 fatal cases of miliary or meningeal tuberculosis seen in the army from 1939 to 1941.

Except at autopsy, the diagnosis of a late primary infection is difficult, two-thirds of the cases pursuing a silent course. The postprimary hematogenous and bronchial manifestations usually bring the condition to clinical notice. The most frequent forms of benign hematogenous reaction are erythema nodosum and exudative pleurisy; the most frequent malignant form, progressive protracted invasion with terminal meningitis or miliary tuberculosis. Sometimes this type of invasion will be manifest only by some minor disease, as for instance, a localized ileocecal tuberculosis. The disease may spread, also, by other routes than the blood stream. A breaking down of the primary lesion may occur, or a bronchus may be eroded by a mass of caseating tracheobronchial lymph nodes. Malignant evolution of a late pulmonary infection is apparently on the wane; it is characterized by progressive leukopenia and lymphopenia, sustained tachycardia, persistence or very rapid resorption of the infiltrate, and by recurring febrile bacillemia. A first infection in adolescence carries a relatively high mortality, owing to the marked tendency toward hematogenous dissemination at this age. Similarly infection in a lightly infected community carries a high fatality rate; and the occurrence of such infections leads to the presumption of a case of open tuberculosis in the vicinity.

Leitner discusses the clinical phases of late primary tuberculosis. He notes that the majority of patients have symptoms, generally fatigability and cough, rarely expectoration. Fever is present about half the time. Elevation of the sedimentation rate is usual, and the blood picture shows a shift to the left, and sometimes a monocytosis. Clinically the disease is of three types: (1) the clinically and roentgenologically latent form, characterized by a positive tuberculin test only; (2) the clinically latent form with positive roentgen findings; (3) the manifest form, which may run the course of an acute infection. A fourth and rarer form is the clinically manifest form without characteristic

roentgen changes. As a rule no complications occur, but pleurisy or other conditions may be observed. Since routine tuberculin testing is cheap, its use in the schools, army, etc., is advised so that cases in which infection is acquired subsequently to a test may be found and treated.

Wernli-Hässig reports a familial tuberculous infection in some detail; *Stephani* discusses the Weltmann reaction; and *Burckhardt* advocates the use of non-response of the temperature to the sulfonamides as a presumptive sign of tuberculous infection.

Bachmann's first article points out some of the common diagnostic errors, including, of course, failure to have roentgenograms made on patients with chest affections, especially chronic or recurrent ones. His second article has to do with the question of reporting tuberculous and quasi-tuberculous conditions.

Some discussion of the first three articles is printed, and profuse illustrations and roentgen reproductions are included. LEWIS G. JACOBS, M.D.

Features of the Early Pulmonary Infiltration. J. B. Amberson, Jr. Am. Rev. Tuberc. **45:** 660–665, June 1942.

Systematic study of apparently healthy people among whom tuberculosis may be expected to appear is the only means by which the behavior of the earliest lesions of pulmonary tuberculosis can be understood. Observations of such groups indicate that most of these lesions first develop between adolescence and the age of thirty or thirty-five. It seems likely that early infiltration may develop within a few days or weeks in the lung of a previously healthy person and in many or most instances there is reason to believe that there have been pre-existing occult foci which served as points of origin. In young white adults who were tuberculin negative, then became tuberculin positive, and still later developed a pulmonary lesion, failure to demonstrate a typical primary complex roentgenologically was usual. Visible enlargement of the regional lymph nodes is usually lacking in this group, in contrast to the observations in young children. Consequently, it is seldom possible to judge clearly whether the lesion discovered is primary or whether it represents an extension from a primary or an exogenous reinfection.

Most lesions of the early infiltration are predominantly exudative, lobular pneumonic in character. It can be assumed that a tuberculous lesion newly developed in the lung of a previously healthy person is an exudative infiltration and therefore potentially unstable. The striking tendency of the early infiltration is to progress to the point of caseation and excavation, and these changes may be rapid. Usually, systemic effects, such as fever and an accelerated erythrocyte sedimentation rate, are not apparent at the time of the early infiltration and there is often a considerable lag in these effects while the lesion is advancing.

Because of the possibility of rapid change in the appearance of the infiltrate it is routine, on discovering a newly developed lesion in a previously healthy person, to make an examination every week during the first one or two months. The opportune time for securing maximal effects of treatment is in the early phase, preferably before there are any severe systemic symptoms and before secondary bronchogenic lesions have had time to develop. To wait for indubitable evidence of an active lesion usually means that the best chance of cure has been lost. L. W. PAUL, M.D.

Endobronchial Tuberculosis. Its Rôle in Causing Rapid Re-expansion or Atelectasis of the Lung Following Closed Pneumonolysis. O. C. Brantigan, R. Hoffman, and D. F. Proctor. Am. Rev. Tuberc. **45:** 477–483, May 1942.

Occasionally patients are encountered in whom closed intrapleural pneumonolysis is followed by rapid re-expansion of the lung and loss of the pneumothorax space. The accepted explanation for this occurrence is excessive leakage of air through the wounds made by the thoracoscopic instrument. This explanation, the authors regard as incorrect. They believe that the presence of an endobronchial lesion in the main-stem bronchus at the orifice of the branch bronchus or within the lumen of the latter explains the rapid loss of air. After severance of the adhesions there is an increase in the amount of pulmonary collapse and a certain degree of kinking of the bronchus. These two factors, together with the endobronchial lesion and the retained secretion, lead to obstruction of the bronchus. The obstruction, however, is of the check-valve type, allowing ingress of air into the affected lung (or lobe) but preventing its escape. It follows that the subcutaneous emphysema is the result of re-expansion of the lung and not the cause. This also explains why frequent refills fail to prevent re-expansion.

In 4 patients recently seen by the authors this complication occurred and in all subsequent bronchoscopy revealed endobronchial lesions at the orifices of the branch bronchi which had caused partial obstruction.

Routine bronchoscopy is recommended before pneumonolysis is performed, with local treatment of the endobronchial lesion if one is present.

L. W. PAUL, M.D.

The Contralateral Lung during Pneumothorax Treatment. F. L. Jennings and P. M. Mattill. Am. Rev. Tuberc. **45:** 461–466, May 1942.

In order to study the effect of a unilateral pneumothorax on the contralateral lung, the author reviewed all of the roentgen films on a series of patients who had had artificial pneumothorax for a period of four to six months or more. The time of observation varied from less than one year in a relatively few patients to over fifteen years in two or three. In the majority of cases it was two or three years. The lesions in each lung were classified before artificial pneumothorax was induced, and the subsequent changes, particularly in the contralateral lung, were noted. The results are presented in tabular form and show that in a patient with bilateral tuberculosis suitable for pneumothorax on one side, there was a 40 per cent chance that the lesion in the contralateral lung would not change, a 26 per cent chance that it would improve, a 6 per cent chance that it would be unstable, and, finally, a 24 per cent chance that it would progress. A patient with a normal contralateral lung and the involved lung suitable for pneumothorax has a 6 per cent chance of developing tuberculosis in the good lung.

L. W. PAUL, M.D.

Study Concerning Clinical and Anatomic Features of Re-expanded Lungs Which Had Been Collapsed by Pneumothorax for Variable Periods of Time. B. P. Potter. J. Thoracic Surg. **11:** 554–564, June 1942.

One hundred and eighteen cases in which 162 lungs were collapsed by pneumothorax have been studied

from one to eight years after termination of the pneumothorax and re-expansion of the lung. There are no postmortem observations. The cases were divided into groups according to the type, number, and location of cavities. There were very few cavities exceeding 3.5 cm. in diameter. The serious complications of pneumothorax were few in number. There were only 5 cases of empyema. In 109 cases effusions developed, with spontaneous absorption except in 2 instances. The contralateral lung usually improved or showed no change; it rarely showed a spread.

An arbitrary schedule was established for duration of the pneumothorax. Small cavities (less than 2.5 cm.) were collapsed for eighteen to twenty-four months. Cavities of 2.5 to 3.5 cm. were collapsed for thirty to thirty-six months. Cavities of 3.5 to 5 cm. were collapsed for three and one-half years to four years and cavities of over 5 cm. were collapsed five years or longer.

On comparing the extent of the residual lesion in the reinflated lung with that present before pneumothorax the author was impressed with the degree of absorption that had taken place. Except for the recurrences these residual lesions have remained unchanged after re-expansion of the lung in all but 9 cases. In these 9 they calcified or continued to improve.

Re-expansion took place quite readily in all cases and was done gradually over a period of three to nine months. Nine of the 118 patients are working and 20 are ambulant; 5 are under treatment, and 3 are dead.

HAROLD O. PETERSON, M.D.

Tuberculosis in the Merchant Navy. J. E. Wood Brit. M. J. **1:** 716–717, June 13, 1942.

The author opens his article by pointing out the considerable difficulty of obtaining actual incidence figures covering tuberculosis in the British Navy. Statistical investigations, however, bear out the suspicion that this condition is prevalent among seamen. One set of figures gives a rate of 2.37 per thousand, another 9.5 per cent of deaths from tuberculosis, while still another set of data reveals that of the deaths occurring within twelve months after leaving sea-going employment, 20 per cent were due to this disease.

The author makes an appeal for early diagnosis to check this appalling loss of man power, the causes of which, he states, consist in unsanitary washing and sleeping conditions. Early diagnosis is difficult due to inadequate examinations (shipping federation doctors are paid one shilling a head for such work). Mass radiography is pointed out as the greatest aid to early diagnosis yet instituted and it is suggested that if it were possible to apply this system universally the proportion of "pick-ups" would gradually drop to a marked degree and the end-result would be highly gratifying. A plea is also made for reform, wherever possible, in general care of the seamen on duty as regards sanitation and provision of sleeping facilities.

Q. B. CORAY, M.D.

The War and Tuberculosis. Esmond R. Long. Am. Rev. Tuberc. **45:** 616–636, June 1942.

This comprehensive study of tuberculosis in the military and civilian population in two great wars—World War I and the present conflict—is the subject of an editorial in RADIOLOGY for September 1942, and to this the reader is referred for an abstract.

A New Aspect of Dry Pleurisy. J. Smart. Brit. M. J. **1:** 604–605, May 16, 1942.

The author offers a short but convincing description of those cases of dry pleurisy in young people which cause symptoms of malaise, respiratory pain, and dry cough without positive roentgenographic or family history findings. It is usually assumed that such cases are tuberculosis, and a long convalescence is recommended, followed by periodic examination and serial roentgenography. This is not always practicable, however, nor is it always necessary, as has been shown recently in the examination of British recruits. In a series of 24 patients examined with the aid of lipiodol, 5 showed a slight but definite bronchiectasis. The treatment was mainly symptomatic and dietetic and most of the patients were soon able to return to service, at least under a special classification.

Q. B. CORAY, M.D.

Miliary Diseases of the Lung. C. R. Austrian and W. H. Brown. Am. Rev. Tuberc. **45:** 751–755, June 1942.

The authors list a total of 22 conditions in which miliary pulmonary shadows have been seen. These include such widely varying diseases as tuberculosis, sarcoid, pneumoconiosis, leukemia, chronic passive congestion, bronchiectasis, sarcomatosis and carcinomatosis. In these many states the symptoms were usually those of the primary pathological condition, the nature of which was indicated often by the history and by other accessory data. Usually, physical signs were lacking or meager. Not infrequently, the precise anatomical status of the lungs was not suspected prior to x-ray examination. In the majority of cases, proof of the exact nature of the local pulmonary changes was lacking. Consequently, the proof of the etiology of the lesions was presumptive in many cases, being based on the collation of all available clinical and laboratory data.

It is emphasized that the mere association of miliary pulmonary shadows with a systemic disease need not establish a unitary cause for the two. Postmortem examination of a case of myeloid leukemia, for example, showed that the pulmonary shadows were due to tubercles and were not caused by leukemic infiltration. The report also emphasizes the hazards of drawing etiological and prognostic inferences from roentgenographic shadows unsupported by other available diagnostic data and points out that now and again proof of the true nature of the anatomical changes cannot be positive without direct inspection of the lesions.

L. W. PAUL, M.D.

Pulmonary Coccidioidal Disease. R. A. Peers, E. Holman, and C. E. Smith. Am. Rev. Tuberc. **45:** 723–740, June 1942.

In order to emphasize the protean character of coccidioidal infection, the authors present a series of cases illustrating the various changes produced. Primary coccidioidomycosis is an infection showing all grades of severity. It may be completely asymptomatic but there is often an influenza-like illness marked by pleurisy. Erythema nodosum develops probably in only one person in from 20 to 50 who experience this infection; this combination constitutes the so-called "San Joaquin fever" or "valley fever." In some patients the infection in the lungs and lymph nodes is complicated by the development of pleural effusion. This

seems to be a part of the initial infection and the prognosis is usually satisfactory. Less frequently a pulmonary cavity develops, usually fairly soon after the primary infection. The cavity produces few symptoms other than an occasional hemoptysis which is not of sufficient severity to endanger life or even health. Danger of dissemination of the disease from this lesion seems to be slight, even though the fungus may be present in the sputum. Rarely the fungus is not successfully walled off in the lungs and disseminates. Coccidioidal granuloma occurs as an endogenous reinfection but fortunately is rare. The time of maximal danger for the development of this highly fatal form of the disease is soon after the infection is acquired, so that every effort should be made toward safeguarding the individual at the time of his primary infection.

The article is well illustrated with numerous reproductions of roentgenograms illustrating the various types of lesions encountered. L. W. PAUL, M.D.

Significance of the Radiological Manifestations of Erythema Nodosum. P. Kerley. Brit. J. Radiol. **15:** 155–165, June 1942.

Erythema nodosum is an acute febrile illness characterized by a painful, nodular, erythematous rash on the shins and forearms and by joint pains and malaise. The etiology has been the subject of much speculation. The characteristic rash and fever have been seen in association with tuberculosis, syphilis, streptococcal, gonorrheal, and meningeal infections, lymphogranuloma inguinale, leprosy, coccidioidomycosis, and during the administration of bromides, iodides, and sulfapyridine. The condition is now generally regarded as an allergic manifestation provoked by bacterial or chemical toxins. It has been confused with numerous other diseases, which may account for the many theories as to its causation.

The distinguishing features of true erythema nodosum are its seasonal incidence, the majority of the cases occurring between March and June; its occurrence in epidemics, and the fact that it is essentially a disease of children and young adults. The Nordic races are most susceptible.

Patients usually present no pulmonary signs or symptoms. A large proportion of those whose chests are examined roentgenologically show massive enlargement of the bronchial lymph nodes, with or without evidence of inflammation in the lungs. The appearance is identical with that seen in Boeck's sarcoid. The node enlargement usually precedes the pulmonary infiltration. The lung infiltration is of two types. In the first the foci are small, round, or oval, averaging about 3 mm. in diameter. These foci are larger and denser than those of miliary tuberculosis. The other type shows reticular striations radiating from the hila. These do not follow the normal distribution of the vascular system.

The pulmonary infiltrations and the node enlargements slowly disappear with recovery.

The differential diagnosis must take into consideration sarcoidosis, Hodgkin's disease, lymphosarcoma, coccidioidosis, and tuberculosis. The similarity in the clinical course and the x-ray appearances between erythema nodosum and sarcoidosis and coccidioidal granuloma suggest a relationship with these diseases.

Twelve cases are reported, and roentgenograms are reproduced. SYDNEY J. HAWLEY, M.D.

Hemorrhagic Cysts of the Lung: Report of Two Cases in Which Marsupialization Was Done. H. K. Gray and Ira C. Skinner. Surgery **11:** 777–787, May 1942.

Lung cysts, like other parenchymatous cysts, may be of congenital, infectious, mechanical, or neoplastic origin. The symptoms are not characteristic, but recurrent attacks of dyspnea and cyanosis in infants and young children may arouse suspicion of cystic disease. Among adults the condition is usually manifested by some complication, such as infection or rupture into a pleural space. Hemoptysis frequently occurs. Diagnosis is usually made only after roentgen studies.

Various forms of therapy have been suggested. Those cysts which are accidentally discovered and are producing no symptoms require no treatment. Sometimes repeated aspiration is used, particularly in children. Aspiration and introduction of iodized oil have been beneficial in a few reported instances. Thoracotomy and cauterization have been tried. The treatment of choice would be removal of the affected tissue either by lobectomy or excision of the cyst, but this is seldom feasible.

Having made the above observations on the basis of the literature, the authors proceed to report two cases of their own. Their first patient, a man 34 years old, complained of dyspnea of seven months' duration. Thoracentesis had been done elsewhere, several hundred cubic centimeters of blood having been removed from the left hemithorax. The patient continued, however, to experience pain and dyspnea and to cough up clots of old blood. Roentgenograms revealed two large circumscribed shadows involving the greater part of the left chest. Bronchoscopic examination showed some degree of compression of the left lower lobe bronchus, believed to be due to a tumor. An exploratory thoracotomy was done and two globular masses of cystic character were found. One contained a thin, brown, bloody fluid, the other a thick, chocolate-like material. Since removal seemed impossible, the cysts were marsupialized, the edges being brought to the parietal pleura and attached throughout their circumference to the soft tissues of the thoracic wall, about 8 cm. of the 8th and 9th ribs having been removed to permit this procedure. The cavities were packed with petrolatum gauze. Later an empyema developed in the pleural cavity, which was drained following resection of the 5th and 6th ribs, anterolaterally. Films made three months later showed that the cystic cavities were reduced in size.

The second patient was a man 26 years old who gave a history of hemoptysis beginning several weeks previously. Roentgenograms showed a large homogeneously dense mass in the upper posterior part of the left hemithorax. There was some erosion of the 5th rib and the trachea was slightly displaced. A diagnosis of cyst with secondary hemorrhage was made and a thoracotomy was done. The lung was so densely adherent to the parietal pleura that it could not be separated. An aspirating needle was therefore inserted into the cyst, yielding dark bloody material. Since it was not possible, for anatomical reasons, to marsupialize the cyst at the site of exploration, a stab wound was made in the posterior axillary line and the cyst was attached there. Large quantities of dark blood continued to drain from the marsupialized cyst. Late results are not recorded in either case.

JOHN E. WHITELEATHER, M.D.

Circumscribed Intrathoracic Neoplasms. J. Alexander. J. A. M. A. **119:** 395–397, May 30, 1942.

Contrary to the impression prevailing among many physicians and roentgenologists, a majority of circumscribed intrathoracic neoplasms arising within the lung are malignant. Many of those that arise outside the lung are also malignant and the prompt removal, therefore, of such neoplasms, unless they can be proved benign, is of vital importance. Whenever possible, a specimen of tissue for microscopic examination should be obtained by bronchoscopy, esophagoscopy, needle aspiration, or from a metastatically involved lymph node in the neck, axilla, or elsewhere. About 70 per cent of the carcinomas of the lung arise in the large bronchi, from which biopsy specimens may be obtained bronchoscopically. Needle aspiration of intrathoracic tumors for the obtaining of biopsy material is not advisable in most instances.

The position of neoplasms within the chest helps to suggest their nature, but mistaken diagnoses based on this criterion are frequent. Large tumors may so completely replace or displace the adjacent parts of the lung that it is impossible to determine roentgenographically whether they arose within the lung and expanded to the costal, diaphragmatic, or mediastinal wall of the hemithorax, or whether they arose within one of the thoracic walls and displaced the adjacent lung. An induced pneumothorax may show whether or not the tumor lies within the lung. If a tumor in the lower part of the chest, but not in continuity with the diaphragm, descends with the lung during inspiration, it is likely to be of intrapulmonary origin. This is not always true, however, since pleural adhesions or malignant invasion of the thoracic wall may so fix that part of the lung containing the tumor that it will not move appreciably during respiration.

Since benign intrathoracic neoplasms rather frequently undergo malignant alteration, and since those that remain benign tend to cause progressive disability and dangerous complications as they increase in size, the patient's safety requires that all presumably removable neoplasms should be promptly operated on, whether or not a preoperative pathologic diagnosis has been made.

The only proper use of high-voltage roentgen irradiation for a possibly removable intrathoracic neoplasm is as a therapeutic test in case of a suspected lymphoblastoma. As high-voltage roentgen therapy does not completely destroy malignant intrathoracic neoplasms, as the best that can be expected from it is a temporary improvement, and as the frequent practical effect of its use is loss of the patient's chance of cure by complete surgical removal of the tumor, radiotherapy must be strongly condemned except for suspected or proved lymphoblastomas and for palliation in cases of inoperable malignant neoplasms.

Non-neoplastic lesions to be differentiated from neoplastic lesions include aneurysms of the great vessels and heart, diaphragmatic hernia, eventration of a part or of the whole of a hemidiaphragm, megaesophagus, substernal thyroid, encapsulated empyema, mediastinal and Pott's abscesses, echinococcic, congenital, developmental, and acquired inflammatory cysts, a solid or abscessed mass of tuberculous hilar or mediastinal lymph nodes, a circumscribed tuberculous or non-tuberculous inflammatory mass within the lung, atelectasis of a single pulmonary lobe.

CLARENCE E. WEAVER, M.D.

Coarctation of the Aorta. A. D. Irvine. Canad. M. A. J. **46:** 436–441, May 1942.

Coarctation of the aorta is defined as partial or complete stenosis of the aorta at, or close to, the level of the insertion of the ductus arteriosus. It is of two types, infantile and adult. This paper is concerned only with the adult type. The condition is rare, the incidence having been estimated as 77 cases per 100,000 autopsies. Approximately three times as many cases in males as in females are reported. The etiology is unknown.

Resulting pathological changes in the circulatory system include development of a collateral circulation to link the proximal aortic segment with the trunk and lower extremities; cardiac enlargement induced by the added strain on the heart caused by necessity of forcing the blood through a collateral system; dilatation of the aorta proximal to the atresia which may be so great as to form a large saccular aneurysm.

Clinically this condition is not apparent until adolescence or early adult life, when the first symptoms presented may be dyspnea or palpitation on exertion. Palpation in the scapular areas, suprasternal notch, or supraclavicular fossae may disclose pulsating tortuous vessels. Due to obstruction to the free flow of blood to the lower limbs there is an abundant supply to the upper part of the body or head, producing a marked difference between blood pressure readings taken in the arm and in the leg, an important diagnostic feature.

Radiologically, coarctation of the aorta is indicated by a notching or scalloping of the inferior surfaces of some of the ribs, known as Rösler's sign. Supporting evidence is cardiac enlargement. With the patient in the left oblique position the actual constriction in the aorta may be demonstrated fluoroscopically or radiographically.

Three cases of coarctation of the aorta discovered accidentally and confirmed by subsequent clinical examination are reported. M. L. CONNELLY, M.D.

Transposition of the Aortic Arch: Report of Three Cases. J. V. Sparks and D. M. Scrimgeour. Brit. J. Radiol. **15:** 150–153, May 1942.

Three cases of right-sided aorta are reported. Two are probably examples of the development of the aortic arch from the fourth right arterial arch, with the formation of an aortic diverticulum at the termination of the arch on the left. The esophagus is displaced anteriorly and follows a tortuous course through the mediastinum. Though the condition is rare, its recognition is important, as it may be a contraindication to gastroscopy, and the peculiar mediastinal shadows may lead to improper treatment for mediastinal tumor. SYDNEY J. HAWLEY, M.D.

THE DIGESTIVE TRACT

Syphilis of the Esophagus: Two Additional Cases. V. L. Peterson. Southern M. J. **35:** 571–573, June 1942.

Two cases believed to be syphilis of the esophagus are reported. The author believes that this condition is more common than generally supposed. One patient, a 22-year-old white woman, complained of dysphagia and pain during the past year and a loss of 27 pounds in weight. She was relieved of her distress only after

regurgitation of the retained food. She had never swallowed a caustic substance. The serological examination was positive for syphilis, and antisyphilitic therapy gave partial relief. The other patient was a 24-year-old white woman with a two-year history of inability to swallow foods and a loss of 73 pounds in weight. There was no history of having swallowed a caustic. A Wassermann test was positive. Improvement followed antisyphilitic treatment but gastrostomy was required.

The diagnosis in these cases is made purely on a clinical and roentgenographic basis. The roentgenogram shows marked narrowing of the entire lower third of the esophagus in each instance, with pronounced dilatation above.

A brief bibliography is appended.

MAX MASS, M.D.

Resection of the Esophagus for Carcinoma: An Analysis of Experiences in 11 Cases. Y. K. Wu and H. H. Loucks. J. Thoracic Surg. **11:** 516–528, June 1942.

Carcinoma of the esophagus is unusually prevalent in North China, being seen more frequently than carcinoma of the stomach at the Peiping Union Medical College Hospital. Radiation therapy and gastrostomy have been of little value even for palliative purposes. In the past two years 11 patients have been operated upon. In spite of careful selection, all but one had advanced disease, indicating the difficulty in early diagnosis. There were ten males and one female in the series, ranging in age from thirty-nine to sixty-five years.

Three patients died in the immediate postoperative stage. Two died subsequently of some other disease. Six are living and well from one to seventeen months after operation.

The following postoperative complications were encountered: mediastinal abscess, putrid empyema and esophagogastropleural fistula, lung abscess and empyema, bronchopneumonia, tension pneumothorax, infection of the chest wall.

For carcinoma in the middle portion of the esophagus a thoracicocervical resection with a preliminary gastrostomy is the procedure of choice. In tumors of the lower third of the esophagus and cardia of the stomach a thoracicoabdominal resection and esophagogastrostomy with complementary jejunostomy is indicated. With careful preoperative selection and preparation of the patient, the operation is surprisingly well tolerated.

HAROLD O. PETERSON, M.D.

Experiences with Eight Cases of Resection of the Esophagus for Carcinoma. D. B. Phemister. J. Thoracic Surg. **11:** 484–493, June 1942.

The author has carried out resection of the esophagus for carcinoma eight times. Six of the 8 cases were primary in the esophagus and 4 patients in this group survived the operation. Two cases were primary in the stomach and involved the esophagus secondarily. One of this group survived operation. The principal cause of death in the 3 fatal cases was infection of the mediastinum and pleura. One patient is alive and free of recurrence for three and one-third years, another for seventeen months, and another for three and one-half months. One patient died after ten months and another after fourteen months, from recurrence. The ages ranged from 46 to 64 years. There were one female and seven males. Blood transfusions are given in all cases, ranging in amount from 500 to 1,100 c.c. Preliminary gastrostomy is considered inadvisable.

HAROLD O. PETERSON, M.D.

Cancer of the Thoracic Esophagus and the Upper End of the Stomach: Review of 23 Cases That Have Undergone Surgical Exploration. H. B. Stephens. J. Thoracic Surg. **11:** 469–483, June 1942.

Of 23 patients operated on for carcinoma of the esophagus, 5 survived the operation. All but one of these 5 are dead. One patient has now lived twenty-two months without any evidence of recurrence. In 13 of the cases the carcinoma involved the thoracic esophagus and in 10 the cardiac end of the stomach. There were 17 males and 6 females in the series, with an average age of 56.7 years. The cases are thoroughly analyzed from the standpoint of duration of symptoms before diagnosis was made, type of tumor, type of surgery, and end-results. An extensive discussion is presented on anesthesia and details of surgical technic, with many sketches to illustrate the anastomoses. Despite the poor results, the author is still optimistic and believes better results will be obtained.

HAROLD O. PETERSON, M.D.

Diverticula of the Duodenum. J. H. Hershey. J. Missouri M. A. **39:** 134–139, May 1942.

The incidence of duodenal diverticula in the general population is surprisingly high according to an analysis of the literature. Adding the figures from a number of reports and his own, the author found 218 cases in 18,650 gastro-intestinal examinations, or 1.11 per cent. The number found at postmortem examination is even higher, reaching 16 per cent in one reported series. The author reports 16 cases, all but two of which occurred in the second portion of the duodenum.

Duodenal diverticula are classified as primary, when the cause is not known, and secondary, when they are associated with some other condition in or around the duodenum. The primary type is found most frequently in the second portion of the duodenum, along the medial aspect. The sac is thin-walled and seldom larger than one or two centimeters in diameter. Various facts suggest that these diverticula develop at the site of an anatomically weak area in the duodenal wall surrounding the entrance of blood vessels. The author is of the opinion that many are asymptomatic. There are no symptoms which have been found to be typical of this condition. If, however, the diverticulum retains barium and is tender to pressure it should be seriously considered as the cause of the patient's complaints. These usually are concerned with upper abdominal pain. Tenderness in the right upper quadrant is often present and there may be nausea and vomiting, a feeling of fullness, and belching of gas. When a diverticulum of the duodenum is found, other causes for the patient's complaints should be ruled out by adequate study. If the sac retains barium up to six hours and if there is tenderness upon pressure, it should be removed. The results obtained by surgery are encouraging.

The author reports one case in detail.

L. W. PAUL, M.D.

Intestinal Obstruction from Gallstones. H. L. Foss and J. D. Summers. Ann. Surg. **115:** 721–735, May 1942.

The authors review the literature of gallstone ileus for the past two decades and analyze a series of 150 cases, including 140 reported by others and 10 cases of their own. While it is not contended that 140 represents the total number of cases reported in the past twenty years, it undoubtedly covers the majority of them.

The relative incidence of intestinal obstruction from gallstones varies according to different writers from 1 to 5 per cent. In the collected series of 150 cases, there were 130 females and 20 males, a ratio of 6.5 to 1, which closely corresponds to the relative incidence of cholelithiasis in the two sexes. The majority of patients were in the sixth and seventh decades of life.

A gallstone large enough to cause intestinal obstruction very rarely passes *via* the common duct, the most common route being by way of a fistula between the fundus of the gallbladder and some portion of the duodenum. The sequence of events begins with cholelithiasis, followed by ulceration and erosion of the gallbladder wall, pericholecystitis, and fistulous tract formation.

In the collected series of 150 patients, 23, or 15.3 per cent, presented no history suggestive of gallbladder disease; 48 patients, or 32 per cent, gave a history of epigastric pain which could be interpreted as being associated with the process of perforation. After the stone enters the small intestine it may pass spontaneously, but more often it becomes arrested in its course, with production of characteristically intermittent obstructive symptoms. The most frequent site of lodgment is the terminal portion of the ileum.

Features of the symptom-complex are emphasized in the hope that the entity may be more easily recognized, for it is only by early surgical intervention that the high mortality rate can be lowered. In general the picture is that of mechanical ileus. The early symptoms of obstruction may simulate biliary colic, but if there has been a previous history of cholelithiasis the more recent episodes of pain will be described as of a different character. For roentgen study a plain film is of greatest aid, though an opaque enema may be useful for ruling out the presence of an obstructing neoplasm in the colon. Rigler, Borman, and Noble (J. A. M. A. **117:** 1753, 1941. Abst. in Radiology **38:** 631, 1942) are quoted as stating that by properly conducted roentgen studies the almost total failure of specific diagnoses of gallstone obstruction can be corrected to a reasonably high percentage of accurate diagnoses, with inevitable improvement in the recovery rate. The finding at operation of a faceted stone is indicative of possible multiple stones, the presence of which should always be ruled out.

Brief histories of the authors' 10 personally treated cases are included. In this small series the operative mortality rate was 50 per cent, chiefly due, it is believed, to delay in sending the patients to the hospital.

J. A. L. McCULLOUGH, M.D.

Intestinal Obstruction Due to a Gallstone: Report of Unusual Instance. S. C. Harvey and G. J. Connor. Yale J. Biol. & Med. **14:** 501–504, May 1942.

A 70-year-old white woman presented herself to the New Haven Hospital on April 3, 1940, having recently "vomited gallstones." Eight days prior to admission she experienced pain in the back, in the region of the scapula on each side. This persisted and on the following day was associated with dull epigastric distress. On the second day of the illness there was also onset of vomiting. The next four days the patient continued to have pain in the back and epigastric distress, but was free of cramps. There was no bowel movement during this period. An enema given by a visiting nurse returned only liquid but did give some relief.

Palpation revealed an indefinite mass in the right lower abdominal quadrant in the region of the cecum. The abdomen was generally tympanitic with a slight fullness in the right flank. Peristaltic sounds were somewhat increased and an occasional high-pitched tinkle was heard. There was no evidence of jaundice clinically. The white cell count was 18,950 with 75 per cent polymorphonuclears. Urinary findings were essentially negative. Roentgenograms of the abdomen revealed evidence of intestinal obstruction in the right lower quadrant, with upward displacement of loops of the small bowel. No evidence of any foreign body could be seen. The preoperative diagnosis was gallstone lodged in the terminal ileum, producing small bowel obstruction.

On April 5, 1940, two days after admission, the patient was operated upon under local procaine infiltration and cyclopropane anesthesia. Palpation in the region of the right flank, at the level of the anterior superior iliac spine, revealed a mass of considerable size lying within the small intestine. This intestinal loop was delivered into the wound and was found to be the site of obstruction by a foreign body, which, on opening the bowel, proved to be a calculus.

Eighteen days postoperatively, an upper gastrointestinal series revealed evidence of a fistula between the duodenum and the gallbladder. An ileal fistula was also present through the abdominal wound at the site of operation. On May 10, 1940, 36 days postoperatively, the patient complained of pain in the rectum. Rectal examination revealed a large calculus, which was removed together with several small calculi. Repeated abdominal films on May 13 showed air in the cystic, common, and hepatic ducts without evidence of any radiopaque calculi.

The patient was last seen August 5, 1940, at which time she was in good condition.

ANDREW H. DOWDY, M.D.

An Evaluation of Intestinal Suction in Intestinal Obstruction. J. B. Blodgett. Surgery **11:** 739–745, May 1942.

Intestinal suction has been used for almost four years in cases of intestinal obstruction at the Peter Bent Brigham Hospital. For evaluating this method there have been added to the cases treated there such other cases from the American literature as satisfy the requirements of classification.

Two distinct types of intestinal obstruction are recognized: (1) simple mechanical obstruction of the small or large bowel; (2) intestinal obstruction associated with peritonitis. The mortality in these two groups is so different that they must be considered separately in evaluating the results of treatment. "Paralytic ileus" not associated with peritonitis is not included in this discussion. In comparison with series treated without intestinal suction the results show differences which are statistically significant.

Fifty-six cases of simple mechanical intestinal ob-

struction were treated without intestinal suction at the Peter Bent Brigham Hospital between 1933 and 1941. To these are added four series from the literature giving a total of 306 cases with 53 deaths, a mortality of 17.3 per cent. In a collected series of 151 cases treated with intestinal suction, 12 deaths resulted, a mortality of 7.3 per cent.

When peritonitis is associated with intestinal obstruction the mortality is greatly increased. Among 56 cases in which suction was not used there were 41 deaths, or 73 per cent, while among 52 cases treated by suction there were 13 deaths, or 25 per cent. No account is taken of the extent of peritoneal involvement.

A further analysis of the cases of mechanical obstruction in which intestinal suction was not used at the Peter Bent Brigham shows the obstruction to have been due to postoperative adhesions in 28 cases, gallstones in 2 cases, impacted fecaliths in 1 case, and carcinoma in 25 cases. In most of these cases operation was done. The highest mortality occurred following obstruction due to carcinoma. In those cases in which intestinal suction was used, obstruction occurred because of postoperative adhesions in 11 cases, hernia in 1 case, and carcinoma in 7 cases. The single operative death in this group was in a case of carcinomatous obstruction.

Intestinal obstruction with peritonitis was due to numerous conditions. Among the causes listed in the group treated with intestinal suction are appendicitis, perforation of the large bowel, inflammation of the female internal genitals, and total hysterectomy. There were seven such cases with two deaths, both following a rupture of the appendix. In all 7 cases operation was performed.

The authors point out that intestinal suction is an ideal physiologic treatment because it produces an outlet for the intestinal contents at a point just proximal to the obstruction. As the intestine is decompressed, the circulation is improved, the smooth muscle regains its normal tone, and the important function of nutrition may be resumed. When the pressure within the intestine is released, the volume of circulating plasma, which has been shown to be reduced in obstruction, is restored to normal. Also, reduction of the intra-abdominal pressure by depression of the intestine allows normal circulation in the great venous channels and normal diaphragmatic excursion. Preoperative decompression of the alimentary tract by intestinal suction may avoid the necessity of colostomy or enterostomy and presents the operator with undistended bowel of normal thickness and tone. If it is continued into the postoperative period, the intraluminal pressure is prevented and the anastomosis is thus protected.

If there is reasonable possibility of vascular strangulation, intestinal suction should not be resorted to, except as a preparation for immediate operation. Nor should it be used in obstruction of the large bowel, since the tube may require several days to pass the ileocecal valve.

The reduced mortality in the proper use of intestinal suction depends upon successful intestinal intubation and the maintenance of continuous suction. The closest supervision and attention to details are required.

References to papers on the technic of the procedure and results obtained elsewhere are appended.

J. E. WHITELEATHER, M.D.

THE DIAPHRAGM

The Polyarcuate Diaphragm. E. Korol and A. J. Saxton. Am. Rev. Tuberc. **45:** 537–543, May 1942.

When the diaphragm during its inspiratory contraction presents two or more arches on each side of the heart instead of a single dome, it is spoken of as a polyarcuate diaphragm. This phenomenon is observed only in deep inspiration and in the erect position and for this reason is not seen postmortem. It is uncommon in the young and in the presence of inflammatory pleural and pulmonary disease. It becomes frequent after middle age, being more common in males, and is seen in a majority of cases of chronic bronchitis and emphysema. Among middle-aged veterans the phenomenon is seen in 30 per cent of all those reporting for roentgen examination of the heart or lungs, and in 100 unselected cases of bronchial asthma it appeared in 54. The etiology seems to be a combination of embryological factors plus uneven atrophy of various muscle bundles in the diaphragm. The observations of the authors do not bear out the statement that these folds are caused by ridges of the liver. Less pronounced folds in the diaphragm can be seen in visceroptosis and emaciation due to depression of the diaphragm, in obesity and kyphosis due to elevation of the lower ribs, and also in artificial pneumothorax with depression of the diaphragm. L. W. PAUL, M.D.

THE SKELETAL SYSTEM

Traumatic Epiphyseal Separations and Their Sequelae. G. Reimann. Schweiz. med. Wchnschr. **72:** 643–645, June 13, 1942.

This study was based on the patients with traumatic epiphyseal separation seen in the Basle Surgical University Clinic from 1915 to 1940. Thirty patients were rechecked after one to twenty-five years. The observed sequelae were premature ossification, deformities, and arthritic changes. In general the changes were greater the younger the child was at the time of injury.

Of the cases recorded in the literature 5 to 30 per cent have shown growth disturbances; these occur even after anatomical reduction. Practically always severe damage results from epiphyseolysis in the hip joint, leading to shortening of the limb and limitation of abduction and adduction as well as rotation. This may result in a deforming arthritis. Slipping of the lower epiphysis of the femur causes shortening of the bone, and severe injury to the vessels may produce grave complications. In the elbow or knee deformities are produced by a unilateral epiphyseal injury; operative relief may be required. In general the results of slipped epiphyses are no worse than of a comparable fracture.

The most frequent sites of injury in the author's series were the upper humeral epiphysis, the lower radial epiphysis, and the lower epiphyses of both tibia and fibula. Most patients were between the ages of 10 and 18.

Some illustrative case reports are included; two of these showed overgrowth of the ulna following injury to the lower radial epiphysis, and a complicating arthritis. LEWIS G. JACOBS, M.D.

Treatment of Fractures of the Shaft of the Humerus. W. R. D. Mitchell and H. G. A. Almond. Brit. M. J. **1:** 715–716, June 13, 1942.

The author discusses a very simple method of management of fractures of the humerus which has been

used before but is now particularly applicable in war casualties The three common methods, including the one under discussion, are: the shoulder spica, the abduction frame, and the three-splint method. The first obviously is not easy to apply and does not hold reduction. The second requires constant attention, due to the horizontal position required, and is unusually difficult where transportation is necessary. The third however, places the arm at the side of the patient, is easy to apply, and according to the author gives results comparable to any method used. It is described as follows:

A 3-inch Gutter splint is placed over the shoulder; another one considerably longer covers the lateral surface of the arm, and a shorter one opposes this on the medial surface. The elbow is left free to afford traction, and the wrist is supported in a splint.

Causes of displacement are discussed as follows: muscular traction, which is soon corrected by continuous action and gravity; compound fractures, which call for actual shortening accomplished by the use of a sling, and finally untreated fractures several days old. In the last case a three-pound weight is slung near the elbow and left on for three days.

Q. B. CORAY, M.D.

Colles's Fracture: A Study of X-Ray Films Before and After Reduction. J. W. Sever. New England J. Med. **226:** 790–794, May 14, 1942.

This is a study of 199 cases of Colles's fracture in which films made before and after reduction were studied when available, in an attempt to determine the anatomical reposition of the fragments. The surgeon is admonished to exert greater care in the reduction of these fractures and the radiologist advised to take greater pains in the interpretation of each case.

In each film a line was drawn along the center of the radial shaft parallel with the long axis and another through the radiocarpal joint. The joint angle was then measured with the aid of a transparent protractor. The normal angle is about 15 degrees beyond a right angle, the joint surface of the radius facing anteriorly. In 36 cases reduction was to only 90°, and in 24 others there was an average residual deformity of −8.3°. In other words, 60 cases, about 39 per cent of those studied, showed unsatisfactory reduction. In 92 other post-reduction cases the average angle was +10.9°. While this latter is a fairly satisfactory average, individual cases ranged from +5 to 30°.

The greatest fault seemed to lie in improper reduction as a result of lack of knowledge as to the injury and the procedure to follow for reduction. Complete flexion of the wrist is prevented by dorsal tilting of the distal radial articular surface due to inadequate reduction. The essential features in reduction of the fracture are loosening of the impaction, flexion of the dorsally rotated distal fragment, and adduction of the hand.

JOHN MCANENY, M.D.

Non-Traumatic Fractures of the Spine. W. Jaeger. Schweiz. med. Wchnschr. **72:** 513–515, May 9, 1942.

Non-traumatic fractures of the spine are usually a result of tetanic seizures or convulsive therapy, and are most frequent in the thoracic region. A sharp crack may be heard, a point of tenderness may appear, and roentgen demonstration of a fracture of the vertebral body is possible. Clinical symptoms are often very slight. The mechanism is the production of a crushing force by the strong ventral and psoas muscles in a back fixed by the spinal muscles. Two cases, one due to electrical shock therapy and one due to lifting and carrying an unusual weight, are reported.

LEWIS G. JACOBS, M.D.

Calcification of Intervertebral Discs. M. Albert. British M. J. **1:** 666–668, May 30, 1942.

The author offers a concise and interesting exposition on diseases of the spinal discs with a detailed account of a case in which disc disease had advanced to the stage of calcification.

A description of the anatomy of the intervertebral disc is given with diagrams. The following lesions are described: prolapsed nucleus pulposus; anterior annular necrosis, a true senile condition causing ankylosis; generalized degeneration such as occurs in spondylosis deformans; nuclear expansion due to osteoporosis, which occurs in senile conditions and rarefying bone diseases; finally, Marie-Strümpell's disease, which is, strictly speaking, not a condition of the discs but a calcification of the anterior and posterior ligaments.

The case reviewed was that of a man of advanced age with apparent complete ankylosis of the spine following focal sepsis which had resulted in calcification elsewhere. Roentgenograms of the spine showed partial absorption of all discs in the lumbar region and calcification in the intervertebral spaces. The process was described as essentially a calcification of the annulus fibrosus brought about by three factors: an ossifiable medium, a rich source of calcium locally, and a poor blood supply. Presence of focal sepsis is apparently worthy of consideration, though not necessarily of importance.

Q. B. CORAY, M.D.

Common Neurological Syndromes Produced by Pressure from Extrusion of an Intervertebral Disc. K. G. McKenzie and E. H. Botterell. Canad. M. A. J. **46:** 424–435, May 1942.

The intervertebral disc, as the plastic unit in the spine, controls the forces of flexion, extension, torsion pressure, and mechanical shock. It is made up of three parts: cartilage plates, the annulus fibrosus, and nucleus pulposus. Changes in structure throughout life may be due to several causes: (1) age and degeneration, producing changes commonly seen radiologically as osteo-arthritis of the spine; (2) developmental defects, as imperfect disappearance and replacement of notochord or blood vessels, producing adolescent kyphosis, and individual or scattered herniations through the cartilage plates (Schmorl's nodes); (3) trauma, which alone does not seem enough to rupture a normal disc but in the presence of some predisposing degeneration or developmental defect may lead to extrusion of the nucleus or nucleus and annulus; (4) infection and malignant disease. These last, however, seldom involve the discs, because of the absence of blood vessels in the latter. Roentgen evidence of loss of normal disc spacing may be an early sign of tuberculosis in the adjacent bone, as this disease causes erosion of the cartilage plates and they bulge and give way into the bone.

Posterior extrusions of the discs may impinge on the spinal cord or nerves. This condition is most common in the two lowest lumbar discs.

Extrusion in the cervical and thoracic regions is rare. Early diagnosis or exploration is important, especially when there is extensive pressure on the cord. In laterally placed lesions symptoms are of motor and sensory pressure. These lesions, such as spurs or calcified extrusions causing pressure on a nerve root, may be better visualized by oblique views of the cervical spine.

The lumbar syndrome is one of severe sciatica overshadowing any co-existent back pain, the condition being almost always due to pressure on the sciatic nerve roots at the fourth or fifth disc. Roentgen examination rules out other known causes of pressure, such as secondary carcinoma, primary new growths involving bone, tuberculous spondylolisthesis, etc. With proper clinical selection before surgical interference, a myelogram is seldom necessary either for diagnosis or localization of the lesion. The indiscriminate use of lipiodol or thorotrast is discouraged.

M. L. CONNELLY, M.D.

Acute Hematogenous Osteomyelitis. H. Mahorner and A. P. Crain. Ann. Surg. **115:** 790–815, May 1942.

A comparative study was made of a series of 66 cases of primary acute hematogenous osteomyelitis admitted to Charity Hospital, New Orleans, between 1937 and 1940 and an earlier series of 112 cases seen at the same institution from 1930 to 1936. In the more recent group the mortality was 6.6 per cent, a sharp contrast to the 24 per cent mortality for the earlier series. Efforts were made to disclose the variations in methods of management which were responsible for the great improvement in mortality.

Acute hematogenous osteomyelitis is predominantly a disease of the growing years, and is more common in boys than in girls. Its onset is usually sudden, with rising temperature and local pain of increasing severity. The roentgen picture shows no uniformity. During the first week there may be no roentgen evidence of the disease, though roentgenograms furnish a valuable record of its progress. Usually by the eighth to the tenth day there can be seen a slight osteoporosis in a small circumscribed or diffuse area and/or evidence of elevation of the periosteum. Subsequent films reveal rapid dissemination through the bone, the appearance of sequestra, and finally the marks of healing, reappearance of calcium density and sclerosis, with disappearance of the osteoporotic areas. Single bone involvement is more common than involvement of multiple bones.

In discussing the pathogenesis the authors point out that acute hematogenous osteomyelitis is a vascular or an intravascular disease. Its most pronounced features are due to the fact that the etiologic factors responsible for the systemic symptoms and the changes n the bones are initially in the vessels.

The comparison of treatment and its results in the two series of cases led to the following conclusions:

Among the most important features responsible for the higher mortality in the earlier series were: unjustified emergency operation before the patient had been properly prepared, and failure to re-establish normal physiology by fluid and electrolyte replacement and blood transfusions before operations were undertaken. In addition to these factors, new chemotherapeutic measures and immunotherapy have undoubtedly contributed an additional favorable influence in the therapy of the disease. Operation itself performed after proper preparation appeared not to be a deleterious factor, and opening the bone not more harmful than incision and drainage.

Evacuation of pus, whether by simple incision or by osteotomy, would seem to be a favorable measure in the management of the disease. Osteotomy apparently does not influence the extent of bone involvement. An additional measure of extreme importance, from the operative point of view, is vein ligation in cases with repeated positive blood cultures. Immobilization in plaster is a measure of great value and of far greater importance than is usually realized.

Numerous roentgenograms are included showing the disease in the acute stages in various forms. The authors also present a chart showing the distribution of acute hematogenous osteomyelitis in the more recent series of 66 cases with a total of 78 bones involved.

J. A. L. MCCULLOUGH, M.D.

Pathology and Treatment of Osteo-Arthritis of the Hip, with Special Emphasis on Pin Arthrodesis and Cup Arthroplasty. Paul H. Harmon. Pennsylvania M. J. **45:** 948–956, June 1942.

Osteo-arthritis of the hip is often referred to as degenerative arthritis, arthritis deformans, senile arthritis, hypertrophic arthritis, or morbus coxae senilis. It may be primary or secondary to some pre-existing disease or injury. In young persons it may follow coxa plana, slipped epiphysis, septic or childhood arthritis, or a congenital dislocation or anomaly. In the adult the pre-existing factor may be an injury, rheumatoid or septic arthritis, Paget's disease, chondromatosis, or syphilis (painless Charcot type). The primary type occurs in older persons; in this group the hip disorder appears to be a locally accentuated manifestation of a multiple joint disorder. In a series of 94 patients studied by the author 37 (39.4 per cent) were classed as secondary, the rest were placed in the primary group.

Trauma—either a single injury or the repeated trauma of everyday activity—is the important factor in the causation of osteo-arthritis. Other factors, however, some possibly hereditary, must be present, since trauma is not invariably followed by degeneration.

The roentgenographic appearance of an arthritic hip is characterized by a loss of joint space, especially in the weight-bearing portions of the head and acetabulum, by osseous sclerosis, and by the presence of marginal exostoses.

Conservative measures include the use of heat, local applications, drugs, and rest. Either bed rest or protection from weight-bearing may give some degree of temporary relief.

Operative interference affords the only hope of permanent relief. Of the various procedures, fixation of the hip is the most conservative and certain procedure. It is especially indicated in unilateral involvement in persons whose occupation requires prolonged and strenuous use of the limb, in those who must remain ambulatory, and in the aged. For those who desire a movable hip the author prefers to do an arthroplasty, using a lucite cap instead of one of vitallium. Not only is lucite just as unirritating and inert in the tissue as is vitallium, but it possesses the positive advantage of being radiolucent, so that changes taking place in the head may be visualized readily. Arthroplasty is the procedure of choice in bilateral cases.

JOSEPH T. DANZER, M.D.

Roentgenographic Study of Craniofacial Dysostosis. Report of Cases: Nonfamilial and Nonhereditary. M. Arce and F. Arce. Am. J. Roentgenol. **47:** 275–290, February 1942.

The authors review the literature and discuss the classification of the cranial dysostoses and theories as to their etiology. It is their opinion that the cases of pathological dysostosis of the skull are not all included in the affections described by Comby and Pierrot-Lape (Presse méd. **34:** 947, 1926) under the title of "nonfamilial and non-hereditary craniofacial dysostosis," or in the syndrome described by Crouzon under the title "hereditary craniofacial dysostosis" (Ann. de méd. **25:** 84, 1929). Cases have been observed in which there was synostosis with marked change in the form of the skull and perhaps slight deformity of the face without exophthalmos, prognathism, parrot's beak nose, or mental disturbance. Also in sporadic cases with no familial history the syndrome considered to be characteristic of Crouzon's disease has been present.

The authors agree with Isola that the skull pictures are produced by synostosis of sutures in the vault, various sutures being involved in different cases, producing different types of deformity. The skull grows very little in the direction perpendicular to the affected suture, and in an exaggerated way in the direction parallel to it.

Roentgen study of the skull is desirable to determine which of the sutures is involved. It is sometimes difficult to determine whether synostosis of a suture is present, and multiple projections are required. It is considered that a suture does not present synostosis if the inner table shows a line of less density, even though undulating, and the outer table shows a dentate appearance in which the interpenetration of the teeth is not complete. All of the sutures should be studied. Sutures uninvolved by the synostosis may show widening as a result of increased intracranial pressure.

In the majority of cases of synostosis there is a cerebriform and digitiform image in the roentgenogram produced by wasting away of the internal table because of pressure by the cerebral convolutions. This may disappear as the course of the case is followed. Another roentgen characteristic of great diagnostic value is the rugose appearance with zones of hyperostosis which is generally seen at the vault of the skull, alternating often with shadows of atrophy. Very often, particularly in cases of synostosis with oxycephalic skull, the prebregmatic region may be thickened, in spite of the fact that the rest of the skull shows thinning. Frequently, there are changes in the image of the base of the skull, since in the majority of cases it undergoes changes of considerable importance, these depending very much on the form of the skull.

In the authors' cases the sinuses of the face were only slightly developed or were even entirely lacking. The mastoids showed little pneumatization. There was only slight development of the orbit in depth, with rather small facial bones, there being a striking contrast between the great development of the skull and the small face.

The characteristic appearance and the sutures involved in trigonocephaly, scaphocephaly, platycephaly, plagiocephaly, acrocephaly, and oxycephaly are described. Eight cases of pathological synostosis of the vault, the majority of which also showed facial synostosis, are reported. Theories which have been advanced to explain the development of craniofacial synostosis are: the infectious theory of Virchow, the traumatic theory, specific hereditary diseases, changes in the fetal membranes, endocrine disturbance, and defect in the germ plasm. H. H. WRIGHT, M.D.

Solitary Unicameral Bone Cysts. H. J. Jaffe and L. Lichtenstein. Arch. Surg. **44:** 1004–1025, June 1942.

Solitary bone cyst is a lesion distinct from localized fibrocystic disease. It generally occurs in the shaft of a long bone during childhood or adolescence. The upper portion of the humeral shaft is affected in about half the cases. The lesion consists of a single cystic chamber filled with fluid, located in the interior of the shaft and limited by the thinned and expanded cortex. The inner surface of the shaft is irregular and lined with a thin layer of connective tissue. These cysts usually attain a large size before discovery and a pathologic fracture is often the first manifestation. Symptoms are slight, and diagnosis is usually made by roentgen examination.

Typically the location is in the shaft of a long bone near an epiphyseal cartilage plate. The cyst rarely erodes through the intact cartilage, but may invade the epiphysis after fusion has occurred. This point is a good differential feature in distinguishing a bone cyst from a giant-cell tumor, as the latter begins in the epiphysis. Expansion of the shaft and cortical attenuation are demonstrable on the roentgenogram; the medullary space may appear scalloped. No periosteal new bone formation is observed in the absence of fracture. Fracture usually takes place in the proximal portion of the cyst, and tends to heal rapidly. The portion of the cyst above the fracture line often fills with spongy bone on healing. Progress of the cyst may lead to invasion of most of the shaft.

At operation the cortical wall presents a bluish sheen and may be of egg-shell thinness. On incision a clear yellowish or serosanguineous fluid is evacuated. The lining membrane is gray-white. Very little material can be obtained by curettage. Microscopically the cortical wall is composed of loose-meshed osseous tissue with fairly large vascular spaces. A scattering of osteoclasts is present. The lining membrane consists of a few layers of connective-tissue cells.

A number of theories of causation have been advanced, but not proved. Mikulicz's theory that the condition represents a local disorder of bone development and growth appeals to the authors.

Cure may be observed to occur spontaneously after fracture. The best treatment is curettage followed by filling the defect with autogenous bone chips and collapse of the cyst wall. Radiation therapy was unsuccessful in the authors' experience.

LEWIS G. JACOBS, M.D.

Skeletal Manifestations of Thyroid Disease. M. Bodenheimer and I. S. Barcham. Surgery **11:** 710–731, May 1942.

Diseases of the thyroid gland may produce skeletal manifestations of great significance. Neoplasms of thyroid origin, hypothyroidism, and hyperthyroidism are all commonly associated with changes in the osseous structures.

Neoplasms: Thyroid tissue has been found in almost

every part of the skeletal system, destroying and replacing the normal bone structure. When it is malignant, a primary carcinoma can frequently be found in the thyroid gland. In such cases, of which the authors present two examples, the diagnosis is not difficult. The bone lesions appear as rarefied areas on the roentgenogram. When, however, thyroid tissue is found in the bone, with no clinical evidence of thyroid gland involvement, the problem is more complicated. In such cases the bone deposits may be either benign or malignant. The origin of the benign deposits is a matter of controversy, some authorities regarding them as arising from embryonic rests and others as "benign metastases" capable of malignant transformation. The malignant lesions may represent malignant change in aberrant thyroid tissue or a true metastasis from a carcinomatous thyroid gland.

Thyroid neoplasms are to be differentiated from the rarefying bone lesions of multiple myeloma, endothelioma, and hyperthyroidism. The authors present a table of differential features. When the neoplasm is of the pulsating type it may closely resemble an aneurysm, angioma, meningocele, hematoma, or other vascular tumor. The progression of symptoms is, however, more rapid in the case of a thyroid neoplasm, and roentgen evidence of bone destruction is more common. Symptoms of hyperthyroidism are also likely to be present (in 50 per cent of the cases). A case of a pulsating metastatic tumor is reported in which there had been an interval of seventeen years between the operation for the primary thyroid neoplasm and the appearance of the metastatic lesion in the spine.

Hypothyroidism: The skeletal changes of hypothyroidism are of three main varieties: (1) deficient growth in the young due to retardation in centers of ossification; (2) retardation of osteoid tissue replacement and ossification in adults; abnormal changes in the epiphyseal plate and epiphyses (juvenile chondroepiphysitis). Only the last two are considered in this review.

Although it is commonly believed that hyperthyroidism which has its inception in adult life does not produce skeletal changes, it must be remembered that the thyroid deficiency is manifested by a general metabolic disorder, in which all the endocrines play a part. Skeletal changes otherwise unaccounted for may be regarded as a result of the generally disordered metabolic state. A case is reported in which there was marked decalcification of the spine, with a metabolic rate of minus 19 and minus 21.

The group of hypothyroid cases with epiphyseal manifestations at the hip joint is of importance because of the difficulty in differentiation from Legg-Calvé-Perthes disease. There are two important differences which serve to distinguish the stippled epiphysis of hypothyroidism from the latter disease. (1) In the epiphyseal plate a layer of bone is formed, consisting of bony trabeculae. (2) In the epiphysis there exist, from the earliest growth period, a number of centers of bone growth or ossification which never coalesce and which are separated by an abnormal type of cartilaginous structure. This is in direct contrast to Legg-Calvé-Perthes disease, in which, prior to onset, there is a single center of ossification in the epiphysis, from which normal bone growth advances.

In hip involvement as a result of hypothyroidism stippled epiphysis is usually bilateral, while in Perthes disease it is usually unilateral. The presence of roentgenographic abnormalities in bones other than those about the hip, such as the knee and ankle, also serve to stamp the disease as endocrine in nature. No evidence of a destructive process is found in hypothyroid stippled epiphysis as in Legg-Calvé-Perthes disease, although this feature is often difficult to distinguish. Response to thyroid therapy is a further diagnostic sign.

An illustrative case is reported, with roentgenograms of the pelvis at various stages of the treatment.

Hyperthyroidism: The changes taking place in the osseous system as a result of hyperthyroidism are of a different type from those discussed above. The skeletal manifestation of the disease is osteoporosis, with any of its attending complications. The osteoporosis is generalized but appears earliest in the small flat bones and the spine and latest in the long bones. The loss of calcium from the bone has been shown to be associated with a negative calcium metabolic balance. There is also a negative phosphorus balance. The serum calcium and phosphorus remain normal. Serum phosphatase values are only moderately high. The calcium excretion has been shown to be dependent upon three principal factors: duration of the disease, rate of calcium loss, and daily calcium intake. The disease is usually of four or five years' duration before bone changes become evident. In one case in the literature it was seventeen years before they were clinically demonstrable. A case is reported by the authors.

The paper concludes with the following paragraph on treatment: "With thorough knowledge and understanding of the bone lesions described, treatment may be attempted on a more rational basis. Needling of so-called aneurysms of the spine will be attempted less often when one realizes that these lesions are often due to a thyroid metastasis. Thyroid substitution therapy in cases of stippled epiphyses is a great aid when definite evidence of hypothyroidism is established. Osteoporosis due to hyperthyroidism is sometimes benefited by thyroidectomy."

J. E. WHITELEATHER, M.D.

Paget's Osteitis Deformans and Hyperthyroidism. Ernst Lyon. Schweiz. med. Wchnschr. **72:** 592–596, May 30, 1942.

Constant metamorphosis of the bones occurs during life. In hyperparathyroidism, hyperthyroidism, and Paget's disease the osteoclastic phase is emphasized; in hypothyroidism there is often an increase in bone calcification. In hyperthyroidism, in contrast to hyperparathyroidism, there is an elevation of blood calcium and serum phosphatase with no hypophosphatemia or acidosis. Several years of hyperthyroidism are necessary to produce bone demineralization.

Experiments (E. Schneider) have shown that a shortage of vitamin A predisposes to thyrotoxic osteoporosis; vitamin D also acts as a regulator of bone structure. Vitamin A and thyroxin act as antagonists.

While progressive bone atrophy is the rule in hyperthyroidism, Paget's disease is a rarer finding. Previous investigators have noticed thyroid enlargement in a large percentage of patients with Paget's disease.

In Paget's disease the blood calcium is generally normal, the serum phosphatase elevated, and the vitamin A excretion elevated. The blood cholesterol is also high. Paget's disease is brought to clinical manifestation in predisposed persons by failure of

vitamin A metabolism in the liver. The presence of other diseases, thyrotoxicosis especially, may act as a predisposing cause for this failure.

The indicated therapy seems to be intensive administration of vitamin A and correction by irradiation of the thyrotoxic state; the Paget's disease is often brought to a state of remission in this way.

LEWIS G. JACOBS, M.D.

OBSTETRICS AND GYNECOLOGY

Use of X-rays in Obstetrics. H. V. Hartzell. West. J. Surg. **50:** 271–281, June 1942.

In prefacing this paper, which presents a comprehensive summary of the subject of x-rays in obstetrics, the author quotes the work of Hodges and Dippel, Stein and Arens, and Horner, to prove that ordinary diagnostic x-ray procedures are harmless to both mother and fetus, and further that all reported cases of x-ray trauma in pregnant women were secondary to therapeutic dosages.

X-ray examination in pregnancy is indicated (1) when vaginal examination is contraindicated, as in patients reporting too late in pregnancy; (2) when the patient is extremely obese; (3) when clinical examination suggests an abnormality in the size or shape of the pelvis; (4) in cases where there is a previous history of dystocia or fetal death; (5) in cases of fractured pelvis; (6) in elderly primiparas; (7) in dystocia during labor, to localize the site of arrest; (8) when requested by the patient; (9) in the android type of pelvis.

The information to be gleaned about the fetus and its status is great. First there is the determination of pregnancy itself. The skeletal centers can usually be made out in sixteen to eighteen weeks. The maturity of the fetus can be estimated either from the length of the fetal skeleton, the fronto-occipital diameter, or the presence or absence of certain ossification centers. The presence of the osseous nucleus of the distal femoral epiphysis is supposed to indicate a full term development. Multiple pregnancy, fetal anomalies, as anencephaly, hydrocephaly, etc., and fetal death can be diagnosed (Schenck's signs). Fetal position and presentation are accurately portrayed and rare cases of abdominal pregnancy can be diagnosed.

Abnormalities of the maternal soft parts also are demonstrable. Use of soft tissue technic has revealed a wide variety of abnormalities in placental implantation. Ude's technic for placenta praevia, where the visualized bladder is shown to be separated from the fetal head more than 2 cm., is described. Hydramnios and abdominal calculi or tumors may also be diagnosed.

The determination of the status of the maternal bony pelvic architecture is the third and a most important phase of x-ray studies in obstetrics. Following the work of Caldwell, Moloy, and Swenson, the author stresses the study of the shape of the pelvis as a whole rather than of isolated measurements. The four main types of pelvis, gynecoid, android, anthropoid, and platypelloid are described. The four principal methods of x-ray pelvimetry are discussed. The author feels that the triangulation method and direct comparison method are the simplest and most practical. The following routine positional studies are made:

(1) Film of inlet, taken with patient sitting so that the superior margin of the symphysis pubis and the 4th lumbar spinous process are equidistant from the table. The plane of inlet should then be parallel to the film.

(2) Lateral view.

(3) Film of the subpubic angle, taken with the patient supine and the tube angled 33° toward the head and centered just below the lower border of the symphysis pubis.

In the study of extrapelvic problems, such as pulmonary and cardiac pathology, physiologic and pathologic changes in the urinary tract, hernia of the esophageal orifice, etc., x-ray studies are invaluable.

SIMON POLLACK, M.D.

THE GENITO-URINARY TRACT

Hydrocelogram, the Roentgenographic Visualization of Hydrocele. S. E. Last. Urol. & Cutan. Rev. **46:** 355–358, June 1942.

The author describes a technic for the demonstration of hydrocele, studied on fresh autopsy material and clinically. In the autopsy studies 5 per cent potassium iodide solution was injected into the tunica vaginalis prior to taking anteroposterior and lateral roentgenograms. An oblique view was taken if the epididymis were situated behind the testis. The testis appeared as a negative shadow capped by the epididymis. The tunica vaginalis was filled with contrast material.

Clinically, neo-iopax or skiodan was used as a contrast medium, being injected after withdrawal of fluid. Satisfactory results were obtained by injecting 10 c.c. of dye for one ounce of fluid removed and 20 c.c. of dye for three ounces of fluid removed. The author believes that the interval between injection of the medium and surgery has no untoward effect on healing.

Eight cases of hydrocele demonstrated by roentgenograms are presented.

When conservative measures for the treatment of hydrocele are used, such as sclerotherapy, it is to the physician's advantage to have a complete picture of the type of hydrocele with which he has to contend; to know, that is, whether it is simple, multilocular, infantile, hourglass, or congenital funicular. In closed operation for epididymitis (Ash-Rhode), this procedure is of great help in locating the epididymis.

MAURICE D. SACHS, M.D.

Urinary Obstructions in Infants and Children. M. F. Campbell. Pennsylvania M. J. **45:** 783–789, May 1942.

At least 90 per cent of all major urologic problems in children are concerned with urinary obstruction and infection. Most of the obstructive lesions are congenital and may be the direct predisposing factor in acute and chronic infection, disturbances of urination, hydronephrosis, hydroureter, or distended bladder.

The author has grouped the types of obstructive lesions, both congenital and acquired, and discusses their progress and method of treatment.

JOSEPH T. DANZER, M.D.

TECHNIC

The Pharmacological Actions of Some Contrast Media and a Comparison of Their Merits. M. Weatherall. Brit. J. Radiol. **15:** 129–137, May 1942.

Seven substances were tested for their action upon the heart muscle, blood pressure, and brain for the

purpose of determining which was the most suitable for use in cardiography and angiography. Only three of the substances are suitable and in common use, diodrast, neo-iopax, and hippuran.

Diodrast in concentrations of greater than 0.4 per cent increased the amplitude of the isolated auricular muscle and increased the beat of the perfused heart and dilated the coronary vessels. Neo-iopax in concentrations of 0.6 per cent or more diminished the beat of the heart and dilated the coronary vessels. Very large doses caused the heart to stop beating. Hippuran caused a small diminution in amplitude.

Diodrast and neo-iopax acted alike on the blood vessels, causing a dilatation with drop in blood pressure. If the drugs were injected rapidly there was a momentary contraction of the blood vessels, probably the result of the irritant effect of the drugs.

All three drugs exerted a similar action when injected into the cranial circulation. Sometimes there was no particular reaction. Occasionally there was a prolonged reaction consisting of rapid, deep irregular respirations, gradual rise in blood pressure, salivation, pupillary changes, and convulsions. If the convulsions were severe the animal died. The three drugs were not equally convulsant; 0.5 c.c. or more of 69 per cent hippuran was always fatal; 1.0 c.c. of 75 per cent neo-iopax caused some convulsions, but lesser amounts never produced convulsions; no reactions occurred after 1.0 c.c. of 70 per cent diodrast.

From these experiments it appears that diodrast is the drug of choice for cranial angiography and either diodrast or neo-iopax is satisfactory for peripheral angiography and cardiography.

SYDNEY J. HAWLEY, M.D.

RADIOTHERAPY

MALIGNANT TUMORS

Effect of Orchiectomy and Irradiation on Cancer of the Prostate. C. Huggins. Ann. Surg. **115:** 1192–1200, June 1942.

The relationship of function of certain endocrine glands to prostatic carcinoma was first demonstrated by Huggins and Hodges, who showed that growth of this cancer is frequently inhibited by eliminating the testicular androgens by bilateral orchiectomy or by neutralization of androgenic activity by estrogen administration, and that, conversely, cancer of the prostate is activated by injection of androgens. It is shown by these same workers that prostatic carcinoma resembles adult prostatic epithelium rather than tissue of more primitive nature and exhibits a similar response to a modification of the androgenic hormonal status.

The present paper reviews the results of treatment of carcinoma of the prostate by surgical excision of the testes and presents 2 cases in which irradiation of both pelvis and testes was employed.

In a series of 45 consecutive patients with advanced prostatic cancer in whom the primary treatment was bilateral orchiectomy, there were 8 deaths, all in patients with metastasis to bones; in 4 of these cases carcinomatosis was the principal cause of death. In 5 patients castration caused no clinical improvement; in 9 there was temporary improvement, and in 31 cases a sustained inhibition of the disease, lasting at least thirty months.

The tumors included adenocarcinoma and undifferentiated carcinoma. The results in the adenoma cases were superior to those in the patients with undifferentiated carcinoma. The latter group accounted for all the deaths from carcinomatosis and the failures to show improvement. The finding of testes much lighter than the usual weight of 20 gm. signified a poor prognosis.

It is of interest that in 5 cases there was a great decrease in the size of the primary neoplasm, while the metastases continued to progress.

Estrogen administration was not found to be a useful supplement in cases which failed to respond to orchiectomy.

Roentgen irradiation of the testes in the two cases described produced atrophy of the germinal epithelium, but not of the interstitial cells of the testis. It is therefore ineffective in controlling the secretory function of the testes and is inadequate as a therapeutic agent in prostatic cancer. J. A. L. MCCULLOUGH, M.D.

Neuroblastoma (Sympathoblastoma or Neurocytoma) of the Suprarenal Medulla; Report of Three Cases. R. M. Thompson. Ann. Int. Med. **16:** 1206–1220, June 1942.

Tumors derived from the sympathetic nervous system of the suprarenal medulla are of three well defined pathologic types: (*a*) neuroblastoma (sympathoblastoma or neurocytoma); (*b*) ganglioneuroma (neuroma ganglionare); (*c*) paraganglioma (chromaffin-cell tumors). In this paper the discussion is limited principally to the neuroblastoma, which occurs chiefly in infants and children and is invariably fatal.

The author reviews the literature on suprarenal neuroblastomas from the time of Virchow (1864), including a discussion of the embryology of the suprarenal gland. Two distinct clinical syndromes caused by the tumor have been described, based upon the location of the metastatic lesions. These are termed the Pepper and Hutchinson syndromes and practically all writers attempt to classify their cases in one or the other of these groups, though the reasons for this are not clear.

Pepper (Am. J. M. Sc. **71:** 287, 1901) described 6 cases of neuroblastoma of the suprarenal medulla which he called round-cell sarcoma or lymphosarcoma. One of these cases was his own and the other 5 he collected from the literature. These 6 cases all occurred in females from three to eleven weeks of age and all showed liver metastases. None of them metastasized to bone. Three cases were primary in the right gland, one in the left, one was bilateral, and in one case the location was not recorded. On this basis, neuroblastomas of the suprarenal in very young infants, with liver metastases only, are usually classified as of the Pepper type.

Hutchinson (Quart. J. Med. **1:** 33, 1907) described 10 cases of suprarenal "sarcoma" in children from three months to nine years of age and emphasized the fact that metastases occurred in the bones of the skull and that all cases occurred spontaneously after trauma. He noted the presence of ecchymosis of the periorbital soft tissue followed by exophthalmos, tumor of the orbital bones, and metastases to the auricular and submaxillary lymph nodes. He described a secondary anemia in all cases but did not mention the leukocyte

picture. At autopsy a tumor of the suprarenal medulla was found on the left side in 6 cases and on the right in 4, the growth varying in size from that of a small walnut to that of a child's head. Hutchinson mentioned that metastases may be found in the ribs, sternum, and vertebrae, but was doubtful as to their presence in the long bones.

About 220 cases of suprarenal neuroblastoma have been reported in the literature; 3 additional cases are presented by the author, 2 in young children and 1 in a boy of 18. Reviewing the published cases and studying his own, he concludes that too much emphasis has been placed upon the so-called clinical syndromes of Pepper and Hutchinson. The histologic picture in the two types is identical, and there is much overlapping of the criteria in the cases recorded. In about 20 per cent a definite classification is impossible. Sex is not a factor in the incidence of these tumors and, in general, the younger the patient, the more undifferentiated are the tumor cells and the greater is the degree of malignancy. The symptoms depend entirely on the position, size, and extent of the primary tumor, together with the location of the metastases. The usual clinical course is progressive, with a rapidly fatal termination. The tumor is sensitive to irradiation, contrary to general opinion, and this treatment prolongs the course, but does not halt metastasis. Although one case is reported in the literature with survival fifteen years after surgical removal of the suprarenal tumor, it is generally concluded that surgery is not of benefit.

J. A. L. McCULLOUGH, M.D.

"Field-Fire" and Invasive Basal Cell Carcinoma—Basal-Squamous Type. J. B. Brown and F. McDowell. Surg., Gynec. & Obst. **74:** 1128–1132, June 1942.

The authors attach the clinical descriptive term of "field-fire basal cell carcinoma" to the variety of tumor which presents a slowly advancing active edge and a center that is free of involvement. Its appearance is likened to a field fire, which actively burns in an advancing circle, leaving a burned-out inactive center. Nothing is characteristic about the microscopic appearance of the cells. Recognition of the extent of the lesion and its treatment by wide excision or radiation are necessary for proper management.

The invasive type of basal-cell carcinoma also lacks distinguishing microscopic characteristics, the term invasive being of clinical significance only. This type appears in the form of small lumps which soon ulcerate and may grow slowly for many years. They may, however, take on rapid growth characteristics and invade widely, though they seldom metastasize. Firmly established on the nose, about the orbit, or deep in the ear region, these tumors are practically incurable.

The basal-squamous type of carcinoma may constitute as high as 20 per cent of supposedly pure types of epithelioma. It is the result of metamorphosis of basal-cell epithelioma and not of roentgen therapy. It may metastasize, is relatively radioresistant, and requires a guarded prognosis.

IVAN J. MILLER, M.D.

Study of Lymphosarcoma and Leukemias, Including Two Chloromas. L. L. Griffin and P. Brindley. Texas State J. Med. **38:** 22–26, May 1942.

The authors list 5 cases of lymphosarcoma and leukemia coming to necropsy in the Department of Pathology of the University of Texas between 1892 and 1922, during which time 1,535 autopsies were performed. In 3,865 autopsies performed since 1922, 25 cases, including related conditions, were discovered and it is upon these that the present paper is based.

The cases are classified in 4 groups. The first, or lymphosarcoma, group included 6 cases, 3 of the small-cell and 3 of the reticulum-cell type. There were 7 chronic leukemias—all myelogenous—constituting the second group, and 8 acute leukemias making up the third group. The fourth group includes 1 case of leukosarcoma, 2 cases of chloroma, and 1 of Hodgkin's disease with a blood picture suggesting eosinophilic leukemia. Brief histories of the cases constituting this last group are included. Details of the other groups are presented in tabular form. The author does not mention treatment except to say that one of the cases of lymphosarcoma responded favorably to irradiation, leading to a clinical diagnosis of Hodgkin's disease.

Neoplastic and Related Conditions in the Bones of Children. C. F. Geschickter. Rhode Island M. J. **25:** 98–101, May 1942.

Because of recent progress in the control of infections and metabolic diseases, neoplasms of bone and related conditions have come to account for an increasing proportion of the diseases of childhood. The author discusses briefly acute and chronic osteomyelitis, Schüller-Christian disease, Gaucher's disease, osteochondroma, benign chondromas, bone cysts, Ewing's endothelial myeloma, osteogenic sarcoma, secondary bone tumors, and sacrococcygeal chordomas. He recommends irradiation in Schüller-Christian disease (deep x-ray therapy in divided doses); in bone cysts of the giant-cell type (moderate doses); in Ewing's tumor (deep x-ray therapy followed by resection or amputation when possible). Some of the metastatic tumors also are moderately radiosensitive, but a cure cannot, of course, be expected. Similarly irradiation may result in calcification in chordomas but does not halt their malignant course.

Relation of Hormones to the Development of Cancer, W. S. Hastings. Pennsylvania M. J. **45:** 960–964. June 1942.

The experimental study of the relation of hormones to cancer has been an outgrowth of work on hormones in general, and especially of work on the female sexual cycle. The author refers particularly to the production of hyperplasia of certain tissues in response to the action of estrin and progestin; to the structural similarity of estrin to some of the more recently discovered carcinogens; to the inhibition or delay of tumor growth in female mice of a high-cancer strain following removal of the ovaries; to the appearance of cancer in male mice and its increased incidence in low-cancer strain females after injection of folliculin; and to experiments which would indicate that the pituitary hormone also plays a rôle.

While it is impossible to carry out comparable experiments in human beings, studies of the human breast reveal that its behavior is also changed by estrogenic substances, and that the process runs parallel and is similar to that occurring in mice. Under the influence of the normal menstrual cycle the breast is monthly stimulated to some degree by estrin. Occasionally this

effect is exaggerated, with the production of a cystic hyperplasia or even malignant growth.

Referring again to animal experiments, the author says: "There must be at least some tendency to spontaneous mammary cancer, and the normal effects of the estrogens must be induced and maintained for a considerable time in the glands by relatively strong stimuli in order to demonstrate clearly an effect on tumor incidence. Furthermore, a certain proportion of the mice of these strains develop cancer with no more estrogenic stimulus than that furnished by their own ovaries and many human mammary carcinomas occur without any sign of a precursory cystic disease. It seems apparent that something additional takes place—something irreversible and something for which estrogenic activity and the heredity factor merely set the stage. . . . The nature of this additional step continues to be the enigma of cancer."

It may be concluded, to quote again, "that some hormones play a part—perhaps an almost essential part—in preparing the soil for the development of certain cancers, but that the effectiveness of their action is proportional to some rather large multiple of their dosage and that there are other factors which are also essential."

Incidentally the author points out that, while estrogens may be given for the relief of symptoms due to their deficiency, excessive doses should be avoided.

JOSEPH T. DANZER, M.D.

BENIGN TUMORS

Management and Treatment of Pituitary Tumors. L. J. Adelstein. West. J. Surg. **50:** 230–237, May 1942.

The author presents five cases of pituitary tumor and discusses the treatment. The first patient was a woman presenting the picture of moderately advanced acromegaly. Repeated series of high-voltage x-ray therapy were given over a period of eight years, a total of 38,000 r units, with no ill effects. The patient was in excellent condition at the time of the report, being still under observation. The following additional cases are described:

Case 1: Moderately advanced pituitary tumor with acromegaly, chromophil adenoma (unverified). Severe incapacitating headaches and failing vision. Immediate and striking improvement following two courses of irradiation.

Case 2: Pituitary tumor with advanced degree of acromegaly, chromophil adenoma (unverified). Moderate enlargement of sella turcica. No headache or visual disturbances. Large thyroid adenoma and symptoms of cardiac failure. Clinical improvement following high-voltage therapy.

Case 3: Large pituitary tumor, probably chromophobe adenoma (unverified). Beginning constriction of visual fields with impairment of visual acuity. Improvement of vision and visual fields and relief from headache following high-voltage therapy.

Case 4: Large intrasellar tumor, preoperatively diagnosed as pituitary tumor with hypopituitarism. Operation with removal of large tumor and release of pressure from optic chiasm. Visual acuity left eye improved from 15/200 to 20/70 and field enlarged. Right eye remained blind. Tumor verified as meningioma.

In summary the author concurs with and quotes Grant (J. A. M. A. **113:** 1279, Sept. 20, 1939):

"The effect of roentgen treatment is beneficial in a sufficiently high percentage of pituitary adenomas to warrant its use preoperatively. In visual field studies an accurate and easily verified control of the results of roentgen therapy is available. Three weeks' treatment should be administered with careful perimetric field examination at the end of that period; only if the visual acuity and fields are unimproved at the end of that period is surgical intervention justified. Postoperatively, roentgen therapy seems definitely to prolong the period before evidence of recurrence of the adenoma appears." SIMON POLLACK, M.D.

Keloids and Their Treatment. L. H. Nason. New England J. Med. **226:** 883–886, May 28, 1942.

A keloid is defined as an exaggerated growth of scar tissue, occupying an intermediate position between normal repair and actual neoplastic change. It is characterized by a tendency to recur, extension beyond the site of the original injury, and projection above the level of the surrounding skin.

The cause is always trauma but only certain people are affected. Keloids rarely occur on the face, forehead, hands, feet, front of the neck, axillae, inguinal and anal regions, and perineum, but they are common around the ears, sides and back of the neck, abdomen, and chest. They are seldom observed in hairy regions.

There are many methods of treatment. Surgical excision with plastic repair alone or followed by moderate irradiation, irradiation alone, and pressure are the methods of choice. Numerous ingenious devices for plastic repair are used. Old, well developed keloids are radioresistant but recent lesions respond well to radiation. The best results are obtained with excision followed in three to five days by irradiation. Pressure alone gives good results but this is applicable in only certain parts of the body and it must be maintained for a long time. JOHN MCANENY, M.D.

TECHNIC

A Method of "Dose-Finding" for Combinations of Rectangular Radiation Fields. C. W. Wilson. Brit. J. Radiol. **15:** 145–149, May 1942.

Measurements of radiation distribution throughout one quadrant were made in a pressd-wood phantom for various sizes and shapes of rectangular fields. Isodose curves were then plotted upon transparent sheets, and mounted in a radial manner on a fixed axis, so that the dose in three dimensions could be determined. This is accomplished by mounting the curves in a special device and using light pointers to locate various points in the space diagram. Isodose curves may be obtained thus for planes at any angle to the central axis. SYDNEY J. HAWLEY, M.D.

Representation of Deep X-Ray Therapy Beams by Means of Isodose Charts. D. E. A. Jones. Brit. J. Radiol. **15:** 178–184, June 1942.

By means of photographic methods and more careful ionization chamber measurements, it is demonstrated that the isodose curves at present commonly used are incorrect in the representation of the distribution at the edges of the beam. There is a much sharper change than is indicated. This means that a more accurate alignment of the beam is necessary, especially of narrow beams. SYDNEY J. HAWLEY, M.D.

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[1] Incorrectly given as Tyler in abstract.

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